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TUMORS OF ISLET CELLS WITH HYPERINSULINISM; BENIGN, MALIGNANT, AND QUESTIONABLE

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As THE NUMBER of reported cases of hypoglycemia with islet cell tumor increases, one is struck in reviewing the literature by the large proportion of circumscribed tumors removed with relief of symptoms in which the pathologist has been in doubt as to whether the tumor was malignant or benign. The most notable case in point is the first successful operative removal by Roscoe Graham, in 1929, of a tumor thought possibly malignant, reported by Howland, Campbell, Maltby and Robinson[37] (1929). The ten-year follow-up on this case has recently been published by Campbell, Graham and Robinson[13] (1939).

In our own series (Whipple and Frantz,[81] 1935) of eight tumors in six patients, no tumor had seemed to us to have any features suggestive of malignancy, microscopically, other than lack of complete encapsulation. Since then, however, in subsequent cases in our series, the histologic findings in some were definitely suggestive of malignancy. Some of these were listed by Whipple[80] (1938), but without pathologic report. It is the purpose of this paper to present these in greater detail and to analyze the cases reported in the literature to date (December 31, 1939), as far as it has been possible to find them,* with particular reference to possible malignant characteristics.†

To date (December 31, 1939), in this hospital, 16 patients have been explored because of hypoglycemia. In one case, no tumor was found and partial pancreatectomy was performed with some relief. In the 15 cases with tumor, three had two tumors, making a total of 18 tumors for examination. Of these, four showed lack of encapsulation and blood vessel invasion, leading us to fear that they were malignant.

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* The Quarterly Index, at the time this is submitted for publication, is available only through September, 1939.

† The tables and the discussion which follow are limited to those cases in which there were hypoglycemia and islet cell tumor. This necessitates eliminating the following cases, some of which have occasionally been misquoted: Vecchi,[77] 1914; Zanetti,[87] 1927; Fahri and Sedad,[20] 1929; Fedoroff,[21] 1931; Hamdi,[30] 1932; Cottalorda and Escarras,[15] 1933; Berardinelli,[7] 1934; Herman,[34] 1935; Evangelisti,[19] 1935; Bailey and Cutler,[3] 1938; Dubois-Ferrière,[18] 1939.

ABBREVIATED CASE REPORTS OF FOUR INSTANCES OF ISLET CELL TUMOR THOUGHT POSSIBLY TO BE MALIGNANT

Case 1.—Whipple,[80] Case 8 (1938): Presbyterian Hospital No. 510933: A. M., white, male, age 51. Symptoms for one year, characterized by inability to be roused in the early morning, irrationality, psychomotor activity, and amnesia for the attacks. Patient noted food relationship and for six months before admission had been taking sugar and orange

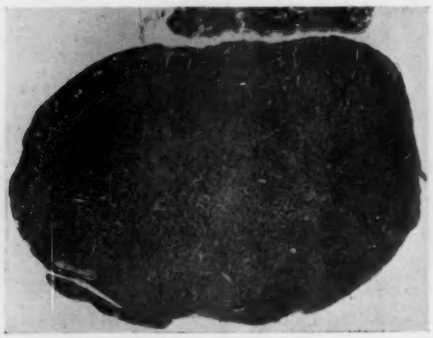

FIG. 1.—Case 1: Low power photomicrograph showing circumscribed tumor and adjacent pancreas. The capsule, microscopically, however, was not complete. Note the fibrosis in the tumor.

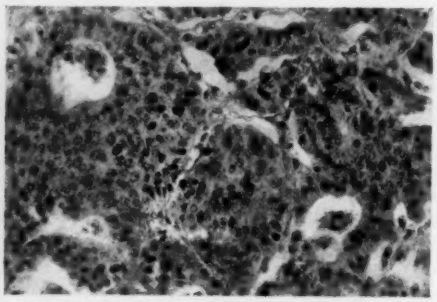

FIG. 2.—Case 1: Higher power photomicrograph showing arrangement of tumor cells, notably around vascular spaces. The cells show some pleomorphism but the tumor is well-differentiated.

juice at bedtime and at 4 A.M. Attacks increasing in frequency. Minimum blood sugar 37 mg. per cent.

Operation.—February 4, 1937: Dr. Allen O. Whipple. No tumor found at first and, therefore, the tail and half of the body were resected. It was then possible to palpate the tumor in the head, and shell it out.

Postoperative Course.—Patient improved for first 36 hours, stated that he felt men-

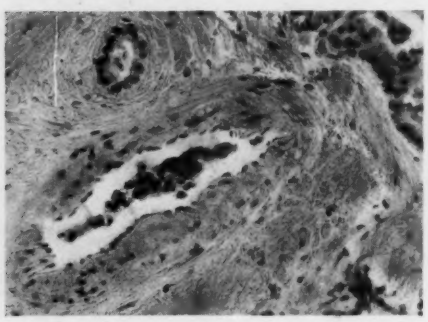

FIG. 3.

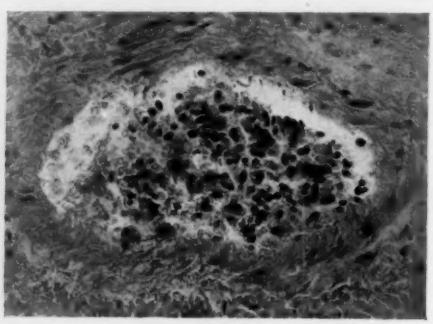

FIG. 4.

FIGS. 3 and 4.—Case 1: Photomicrographs showing tumor cells in blood vessels.

tally clearer, and had no further hypoglycemia. But he developed bronchopneumonia and died, his temperature rising to 108° F., and his blood amylase to 138 units (Myers and Killian method). No autopsy was obtained.

Pathologic Examination.—Gross: Path. No. 63130, Dr. V. K. Frantz. The tumor, apparently encapsulated, measured 1.5x1.0x0.8 cm., and had a thin strip of pancreatic tissue adherent to the capsule. It appeared yellowish, with a faint bluish overtone, and the surface vessels were fine but engorged. On section, it was soft, pinkish-yellow, with ill-defined areas of white fibrous tissue.

Microscopically (Figs. 1, 2, 3 and 4), the capsule was incomplete; tumor cells appeared to invade the surrounding pancreas. The cells, which somewhat resembled the cells of the islands in the adjacent pancreas, were arranged in ribbon-like cords, sometimes

arranged in rosettes about endothelial-lined blood-filled spaces, or about similar spaces lacking an endothelial lining. There was considerable variation in cell size and quite marked hyperchromatism. No mitoses were seen.

Dr. Margaret Murray attempted to cultivate this tumor *in vitro*, but failed, although she had previously obtained excellent growth from an islet cell adenoma, with subsequent graft into a diabetic patient (Murray and Bradley,[60] 1935).

Case 2.—Whipple,[80] Case 10 (1938): Presbyterian Hospital No. 540606: J. S., white, male, age 50. Symptoms for one year, characterized by attacks of confusion, disorientation, and unconsciousness with convulsive movements, with amnesia for the attacks. The episodes occurred chiefly during the early morning. For four months before admission they had increased in frequency and severity. The minimum blood sugar 27 mg. per cent.

Operation.—January 13, 1938: Dr. Allen O. Whipple. Splenectomy and resection of the tail of the pancreas, in which a tumor was palpable.

Subsequent Course.—Patient made good recovery from operation and is free from evidence of disease, 17 months later.

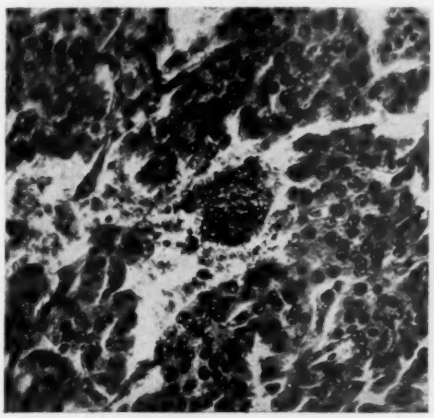

FIG. 5.—Case 2: Photomicrograph showing the general topography of the tumor. Note the large number of vascular spaces, and moderate variability in the cells.

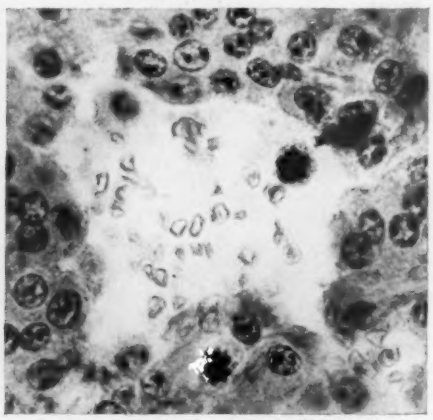

FIG. 6.—Case 2: Higher power photomicrograph showing a vascular space lined by tumor cells; with cells in mitosis bordering the lumen; and one in mitosis, free in the lumen among the erythrocytes.

Pathologic Examination.—Gross: Path. No. 66090, Dr. V. K. Frantz. On the anterior aspect of the specimen of tail of the pancreas submitted, there was a bluish swelling shining through the capsule of the gland. On section, this proved to be an oval, almost completely encapsulated mass of very friable, very soft, dark-purplish tissue. The encapsulation, grossly, was not complete over one small area.

Microscopically (Figs. 5 and 6), the capsule was incomplete. The tumor was composed of cells resembling the cells of the islet tissue in the adjacent pancreas. There were occasionally, however, much larger cells, and numerous mitotic figures. The cells were arranged in broad, wavy bands, separated from one another by irregular spaces filled with blood. Only occasionally could an endothelial lining be observed in these spaces. In at least four instances, cells in mitosis were found directly lining a vascular space, and, in two instances, a cell in mitosis lay free in one of the vascular spaces.

Dr. Margaret Murray cultivated this tumor *in vitro* (Figs. 7 and 8). The growth was much more vigorous than in the tumors previously cultivated and more bizarre. The first epithelial growth was observed in 24 hours, the shortest latent period of any of the tumors. By the fourth day, there was a diffuse growth in most of the cultures. There was some pleomorphism. A striking feature of the first growth was the appearance of large multinucleated cells. These did not reappear after the cultures were transferred. The rapidity of cell multiplication approached the rate of growth of embryonic tissue. Mitoses averaged six to a culture, at any given time.

Case 3.—Whipple, Case 12 (not yet published): Presbyterian Hospital No. 546637: M. O., white, female, age 20. Episodes of fatigue, confusion and dizziness since childhood. A year before admission, attacks of confusion often with complete amnesia usually occurring on awakening, lasting from six to eight hours. No attacks occurred after meals, and relief was obtained by taking orange juice. Minimum blood sugar 26 mg. per cent.

Operation.—April 30, 1938: Dr. Allen O. Whipple. An adenoma was found on the anterior surface of the body of the pancreas near the lower border. This was easily shelled out.

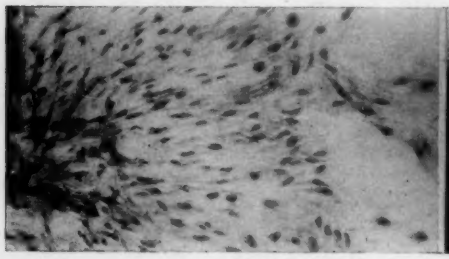

FIG. 7.—Case 2: Photomicrograph of the tissue culture showing epithelium not of the pavement type.

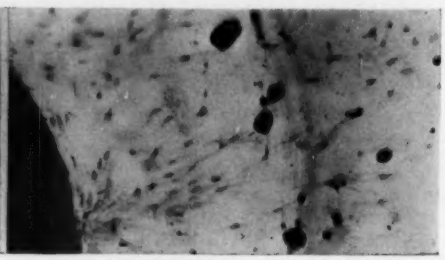

FIG. 8.—Case 2: Photomicrograph of the tissue culture showing multinucleated cells in the first outgrowth.

Subsequent Course.—The patient made a good recovery, and was symptom-free, 13 months after operation.

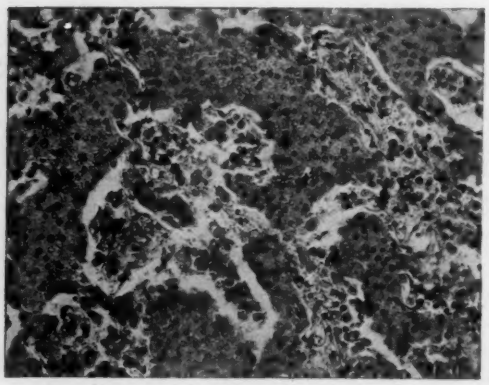

FIG. 9.—Case 3: Photomicrograph of the general topography showing ribbon-like arrangement of tumor and many vascular spaces.

Pathologic Examination.—Gross: Path. No. 67137, Dr. V. K. Frantz. The tumor, apparently encapsulated, was biscuit-shaped, and measured 1.2 cm. in greatest diameter. A small strip of pancreatic tissue was attached. The tumor was soft and reddish. On section, under about one-third of the capsule there was yellowish tissue, suggesting pancreas. The rest of the mass was composed of homogeneous, soft, pinkish-yellow tissue apparently more vascular in the center.

Microscopically, the capsule was incomplete and tumor tissue mingled with pancreatic tissue in a portion of the periphery. The tumor was composed of cells resembling the cells in the islands of the adjacent pancreas. They were slightly larger and the cell outlines were indistinct. They were arranged in ribbon-like, winding cords interspersed with capillary spaces (Fig. 9). There were also many blood-filled spaces directly lined by tumor cells. No mitotic figures were seen. Many of the large blood vessels contained clumps of tumor cells.

This tumor was not cultivated *in vitro.*

Case 4.—Whipple, Case 15 (not yet published): Presbyterian Hospital No. 583832: O. A., white, male, age 46. Symptoms for four years, characterized by fainting spells and amnesia before attacks. The episodes started with blurred vision and dizziness, and the patient noted that exercise precipitated them but did not note any relation to food. No unusual psychiatric behavior and no convulsions. Minimum blood sugar 36 mg. per cent. The patient had been explored one year before admission in another hospital. No tumor was found and no part of the pancreas resected. During the year following operation, he

was considerably benefited by a high carbohydrate diet, with seven meals a day, which resulted in a gain of 18 pounds.

Operation.—June 27, 1939: Dr. Allen O. Whipple. After mobilizing the duodenum and the head of the pancreas, the adenoma was found in the posterior portion of the pancreas near the lower border, between the superior mesenteric vessels on the mesial aspect and the inferior pancreaticoduodenal vessels on the right.

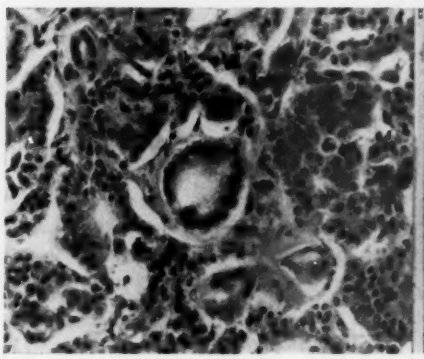

FIG. 10.—Case 4: Photomicrograph of the general topography showing good differentiation; occasional ducts; and many vascular spaces.

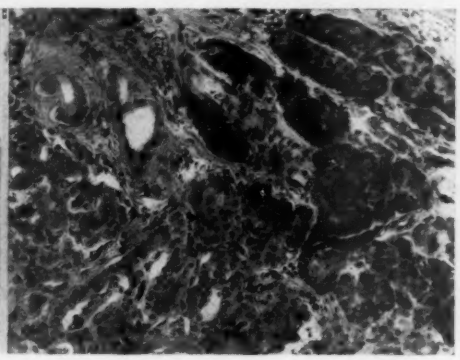

FIG. 11.—Case 4: Photomicrograph of the tumor and adjacent pancreas showing lack of encapsulation.

Subsequent Course.—Patient made a good recovery, and was symptom-free, five months after operation.

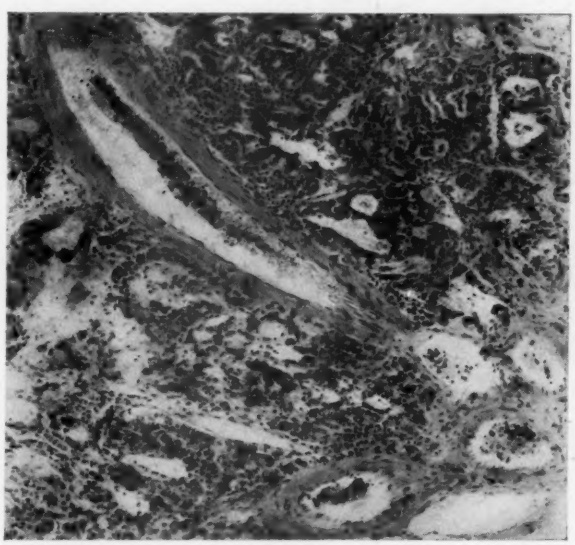

FIG. 12.—Case 4: Photomicrograph showing tumor cells in three different sections of blood vessels.

Pathologic Examination.—Gross: Path. No. 71155, Dr. A. P. Stout. The tumor was irregularly rounded, apparently encapsulated, and dark-pink, measuring 1.5 cm. in greatest diameter. Adherent to the surface of the capsule there was a small amount of pancreatic tissue. On section, the cut surface was soft, delicately homogeneous, and mottled by various shades of red and pink.

Microscopically (Figs. 10, 11 and 12), the tumor, in general, was separated from the pancreatic tissue by a delicate capsule but in a few areas tumor cells appeared to be in

contact with the acinar cells. The tumor was composed of cells resembling those of the normal pancreatic islands. They formed anastomosing cords supported by bands of fibrous tissue in which there were many blood vessels, chiefly capillaries. Occasionally ducts were seen in the tumor. In some of the larger blood vessels masses of what appeared to be degenerated tumor cells were found within the lumen.

No attempt was made to cultivate this tumor *in vitro*.

These four cases have been a great puzzle to us. The postoperative mortality in the first case, in which no autopsy was obtained, left no possibility of further investigation of the nature of the tumor. The second case had all the appearance of a carcinoma microscopically. This patient, in spite of our apprehension, has remained well for 17 months. The last two cases, which appeared less malignant than the second, but which had blood vessel invasion, are symptom-free, 13 and five months, respectively.

There can be no dispute about the malignancy in five published cases of hypoglycemia in which carcinoma of islet cells with metastases was found. It is noteworthy that these were all fulminating cases of short duration. It is also of interest that metastases were found at autopsy in the liver, the lymph nodes, mesentery, peritoneum and epicardium, but not elsewhere. There can be little doubt of the functional nature of the metastases, as illustrated by the

TABLE I

HYPOGLYCEMIA. ISLET CELL TUMORS IN WHICH METASTASES WERE FOUND—FIVE CASES

Author Date	Operation	Result	Pancreatic Tumor Single or Multiple	Capsule	Blood Vessel Invasion	Insulin Extracted	Autopsy
1927							
1. Wilder, Allan, Power and Robertson[82]	Exploratory	Died postop.	Multiple	Not described	Not described	Liver nodule	Metastases in liver, lymph node and mesentery
1934							
2. Judd, Faust and Dixon[44]	Exploratory. Tumor of pancreas and multiple metastases in liver. Biopsy of liver nodule	Died postop.	Single	Original tumor not examined	Original tumor not examined	Not done	Not done
1935							
3. Bickel, Mozer and Junet[9]	None	Died without operation	Single	Not described	Not described	Primary growth. Liver nodule negative	Metastases in liver, peritoneum and epicardium. Interstitial pancreatitis
1937							
4. Cragg, Power and Lindem[16]	Exploratory. Biopsy of liver nodule	Died postop.	Diffuse through pancreas	None	Not described	Liver nodule	Metastases in liver and lymph nodes. Cyst of ovary
1938							
5. Joachim and Banowitch[41]	Resection of spleen and portion of tumor in tail of pancreas and a lymph node showing metastasis. Liver apparently negative	Died postop.	Multiple	Not described	Not described	Not done	Not done

TABLE II

HYPOGLYCEMIA. ISLET CELL TUMORS REMOVED AT OPERATION.
CONSIDERED TO BE BENIGN—46 CASES

Author	Date	Single or Multiple	Capsule Microscopically	Blood Vessel Invasion	Insulin Extraction	Result
1. Mathias[54]	1928	Multiple	Islands in wall of cyst	Not described	o	Mild glycosuria postop.
2. Carr, Parker, Grove, Fisher and Larrimore[14]	1931	Single	Complete	Not described	o	Symptom-free 7 yrs.
3. Tomkies[76]	1932	Single	Not described	Not described	o	Symptom-free 6 yrs.
4. Derick, Newton, Schulz, Bowie and Pokorny[17]	1933	Single	Complete	Not described	+	Symptom-free 5 yrs.
5. Graham and Womack[29]	1933	2 tumors	Not complete	Not described	+	No attacks. Permanent central nervous system damage 5 yrs.
6. Ross[67]	1934	Single	Not complete	Not described	o	Symptom-free 2 yrs., 4 mos.
7. Whipple and Frantz[81] (Case 1)	1935	Single	Complete	None	o	Symptom-free 68 mos.
8. Whipple and Frantz[81] (Case 2)	1935	Single	Complete	None	o	Symptom-free 53 mos.
9. Whipple and Frantz[81] (Case 3)	1935	2 tumors	Both incomplete	None	o	Symptom-free 25 mos. Died of duodenal hemorrhage elsewhere, 27 mos.
10. Whipple and Frantz[81] (Case 4)	1935	2 tumors	Both complete	None	Unsuccessful	Symptom-free 57 mos.
11. Whipple and Frantz[81] (Case 5)	1935	Single	Incomplete	None	o	Symptom-free 59 mos.
12. Whipple and Frantz[81] (Case 6)	1935	Single	Incomplete	None	o	Symptom-free 56 mos.
13. Wangensteen[78] (Case 1)	1935	Single	Not described	Not described	o	Symptom-free 3 yrs., 9 mos.
14. Smith, Hashinger and Engel[72]	1935	Single	Incomplete	Not described	o	Symptom-free 30 mos.
15. Jirásek, Postránecky and Henner[39] (Case 1)	1936	Single	Not described	Not described	o	Symptom-free 2 yrs.
16. Gilmour[28]	1936	Single	Complete	Not described	o	Symptom-free 1 yr., 8 mos. Then fainting spell after influenza. Blood sugar 40 mg. Well since
17. Harnapp[31]	1936	Single	Incomplete	Not described	o	Symptom-free 2 yrs.
18. Liu, Loucks, Chou and Chen[50]	1936	Single	Incomplete	Not described	o	Symptom-free 5 mos.
19. Kepler and Walters[46]	1936	Single	Not described	Not described	o	Symptom-free 2 yrs., 4 mos.
20. McCaughan and Broun[55] (Case 4)	1937	Single	Complete	Not described	o	Not relieved. Re-explored. Resection impossible because of adhesions
21. Herman and Guis[32]	1937	Single	Complete	Tumor completely calcified	o	Symptom-free 2 yrs.
22. Kusonoki and Munakata[48]	1937	Single	Complete	Not described	o	Symptom-free 3 mos.
23. Reiter[65] (Case 2)	1937	Single	Complete	Not described	o	Symptom-free 14 mos. Has Gaucher's disease
24. Lukens and Ravdin[52]	1937	Single	Not described	Not described	o	Symptom-free 1 yr.
25. Kalbfleisch[45] (Case 2)	1937	Single	Complete	Not described	o	Relieved

TABLE II—Continued

26. Kalbfleisch[45] (Case 3) Heupke and Obert[36]	1937	5 tumors	Complete	Not described	0	Died 2 days postop. 4 of 5 tumors found at autopsy. Adenoma of hypophysis and of parathyroid. Hyperplasia of thymus
27. White and Gildea[82]	1937	Single	Complete	Not described	0	Symptom-free 9 mos.
28. Wangensteen[78] (Case 3)	1937	Single	Not described	Not described	0	Symptom-free 19 mos.
29. Fraser, Maclay and Mann[25]	1938	Single	Complete	Not described	0	Symptom-free 5 mos.
30. Jirásek and Postránecky[40] (Case 2)	1938	Single	Not described	Not described	0	Symptom-free 4 mos.
31. Nicholson and Hart[61]	1938	Single	Not described	Not described	0	Symptom-free 18 mos.
32. Parade and Kindler[63]	1938	Single	Complete	Not described	0	Complete recovery
33. Hermannsen and Nestmann[35]	1938	Single	Complete	Not described	0	Immediate relief of hypoglycemia. Died postop. Fever 41° C.
34. Whipple[80] (Case 9)	1938	2 tumors	1 Complete 2 Incomplete	None None	0	Symptom-free 24 mos.
35. Whipple[80] (Case 11)	1938	Single	Incomplete	None	0	Symptom-free 10 mos. Question of pituitary tumor
36. Krauss[47]	1939	Single	Complete	Not described	0	Good recovery
37. Bergonzi[8]	1939	Single	Not described	Not described	0	Died postop. Autopsy: No metastases. Changes in cerebral cortex
38. Murphy, Dustin and Bowman[59]	1939	Single	Incomplete	Not described	0	Relief of symptoms
39. West and Kahn[79]	1939	Single	Not described	Not described	0	Symptom-free 14 mos.
40. Akerberg[2]	1939	Single	Not described	Not described	+	Died fourth day postop. Pancreatitis and peritonitis. 2 colloid adenomata in thyroid
41. Campbell, Graham and Robinson[12] (Case 2)	1939	Single	Not described	Not described	+	Symptom-free 20 mos.
42. Campbell, Graham and Robinson[12] (Case 3)	1939	Single	Not described	Not described	+	Symptom-free 15 mos.
43. Campbell, Graham and Robinson[12] (Case 4)	1939	Single	Complete	Not described	+	Died third day postop. Temp. 107° F.
44. Whipple (Case 13) (Not yet published)		Single	Incomplete	None	0	Symptom-free 14 mos.
45. Whipple (Case 14) (Not yet published)		Single	Incomplete	None	0	Died 56 hrs. postop. Temp. 105.6° F. Appearance that of thyroid crisis
46. Whipple (Case 16) (Not yet published)		Single	Incomplete	None	0	Symptom-free 2 mos.

first and fourth cases (Wilder, Allan, Power and Robertson[83] [1927]; and Cragg, Power and Lindem[16] [1937]).

A review of published cases of tumors removed at operation, and considered benign (with our own series brought up to date), is given in Table II, with a brief abstract of certain features of the pathologic reports. It will be noticed that some cases listed by Whipple,[80] in 1938, are omitted, as these

TABLE III

HYPOGLYCEMIA. ISLET CELL TUMORS FOUND AT AUTOPSY.
CONSIDERED TO BE BENIGN—24 CASES

Author	Date	Single or Multiple	Capsule Microscopically	Blood Vessel Invasion	Insulin Extracted	Autopsy
1. McClenahan and Norris[56]	1929	Single	Incomplete	Not described	o	No metastases
2. Smith and Seibel[73]	1931	Single	Complete	Not described	o	No metastases. Brain normal
3. Terbrüggen[74] (Frank,[26] Case 1)	1931	Multiple	Complete	Not described	o	No metastases. Atrophy of brain. Chronic leptomeningitis. Persistent thymus. Two chief cell adenomata of hypophysis. Liver low in glycogen
4. Buchner[11] (Bielschowsky[10])	1932	Single	Complete	Not described	o	No metastases. Patient a diabetic originally. Cirrhosis of pancreas
5. Barnard[4]	1932	Single	Incomplete	Not described	o	No metastases. Enlargement anterior lobe pituitary. Brain normal
6. Cairns and Tanner[12]	1933	Single	Complete	Not described	o	No metastases. Brain normal
7. Gibbs[27]	1933	Single	Not described	Not described	o	No metastases. Hemorrhagic cyst of adrenal
8. Wolf, Hare and Riggs[84]	1933	3 tumors	Complete	Not described	o	No metastases. Loss of cells in cortical layers of cerebrum
9. Reinhoff and Lewis[68]	1934	Single	Not described	Not described	Not successful	No metastases. Enlarged thymus. Adenomata of anterior lobe of hypophysis. Liver low in glycogen
10. Frank[24] (Case 2)	1935	2 tumors	Not described	Not described	o	No metastases
11. Long, Sheplin and Fishback[51]	1936	Single	Not described	Not described	o	No metastases. Carcinoma of sigmoid
12. Seino[70]	1937	Single	Complete	Not described	o	No metastases. Atrophy of liver
13. Reiter[65]	1937	Single	Complete	Not described	o	No metastases
14. Kalbfleisch[45] (Case 1)	1937	Single	Complete	Not described	o	No metastases
15. Ziskind, Bayley and Mauer[89]	1937	Single	Incomplete	None	o	No metastases. Thyroid normal
16. Jones and Matte[42]	1938	Single	Not described	Not described	o	No metastases. Necroses in brain
17. Malamud and Grosh[53]	1938	Single	Complete	Not described	o	No metastases. Diffuse degeneration of brain
18. Scheller and Stroebe[69]	1938	Single	Incomplete	Not described	o	No metastases
19. Levison and Ramsey[49]	1938	Single	Complete	None	o	No metastases. Fatty degeneration of liver
20. Friedman[28] (Case 1)	1939	Single	Complete	Not described	o	No metastases. Adenomatous hyperplasia of anterior lobe of pituitary. Bilateral cortical adenomata of adrenal. Adenomata of kidney, ileum
21. Friedman[28] (Case 2)	1939	Single	Incomplete	Not described	o	No metastases. Adenomatous hyperplasia of anterior lobe of pituitary and basophilic infiltration of posterior lobe
22. Isaji[38] (Case 1)	1939	Single	Complete	Not described	+	No metastases. Hypophysis and adrenals slightly enlarged. Cyst of parathyroid
23. Isaji[38] (Case 2)	1939	Single with cyst-adenoma	Not described	Not described	o	No metastases. Tuberculosis posterior lobe hypophysis
24. West and Kahn[79] (Case 2)	1939	Single	Not described	Not described	o	No metastases

were personal communications to the author and no microscopic findings were available.

It is interesting that in this series there is only one case with recurrence of symptoms (No. 20), and one with a transitory episode following influenza (No. 16). The case with persistent symptoms has been reexplored but further partial pancreatectomy was impossible because of adhesions. In cases with persistence or recurrence of symptoms, the presence of a second tumor must always be suspected, because of the numerous instances of multiple tumors, some removed simultaneously and others at successive operations.

A review of published cases of tumors found at autopsy and considered benign is given in Table III.

TABLE IV

HYPOGLYCEMIA. ISLET CELL TUMORS REMOVED AT OPERATION. SUSPECTED OF BEING MALIGNANT—19 CASES

Author	Date	Single or Multiple	Capsule Microscopically	Blood Vessel Invasion	Insulin Extracted	Result
1. Howland, Campbell, Maltby and Robinson[37]	1929	Single	Incomplete	Not described	+	Symptom-free 10 yrs.
2. Womack, Gnagi and Graham, E. A.[86]	1931	Single	Incomplete	Not described	–	Symptom-free 7 yrs.
3. Bast, Schmidt and Sevringhaus[5]	1932	Single	Incomplete	Tumor in vessels	–	Symptom-free 8 wks.
4. Judd, Allan, Frank and Rynearson[43] (Case 6)	1933	Single	Not described	Not described	–	Symptom-free 22 mos.
5. Judd, Allan, Frank and Rynearson[43] (Case 7)	1933	2 tumors	Not described	Not described	–	Symptom-free 23 mos.
6. Graham, E. A., and Womack[29]	1933	Single	Complete	Tumor in vessels	–	Symptom-free 5 yrs.
7. Wangensteen[78] (Case 2)	1935	Single	Not described	Not described	–	Symptom-free 39 mos. Mental deterioration
8. Aitken[1] (O'Leary and Womack)[62]	1936	Single	Incomplete	Not described	–	Symptom-free 2 yrs.
9. Rynearson[68] (Case 1)	1936	Single	Not described	Not described	–	Died, postoperative pneumonia. No autopsy
10. Rynearson[68] (Case 2)	1936	Single	Not described	Not described	–	Died, postoperative pneumonia. No autopsy
11. Munakata[58]	1936	Single	Incomplete	None	–	Symptom-free 4 mos.
12. Ziskind and Bayley[88]	1937	2 tumors	Incomplete	Not described	–	Died 32 hrs. postop. Respiration failure. Temp. 107° F. Autopsy. No metastases
13. Whipple[80] (Case 8)	1938	Single	Incomplete	Tumor in vessels	–	Died of pneumonia 5 days postop. No autopsy
14. Whipple[80] (Case 10)	1938	Single	Incomplete	Tumor in vessels	–	Symptom-free 17 mos.
15. Forbes, Davidson and Duncan[22]	1939	Single	Incomplete	Not described	–	Relieved of symptoms
16. Smith[71]	1939	Multiple	Incomplete	Not described	–	Symptom-free 5 mos.
17. Beck and Segrest[6]	1939	Single	Not described	Tumor in vessels	–	Symptom-free 5 yrs., 9 mos.
18. Whipple (Case 12). (Not yet published)		Single	Incomplete	Tumor in vessels	–	Symptom-free 13 mos.
19. Whipple (Case 15) (Not yet published)		Single	Incomplete	Tumor in vessels	–	Symptom-free 5 mos.

A review of published cases of tumors removed at operation, and considered possibly malignant (with our own series brought up to date), is given in Table IV. In none of these, who survived operation, has there been any recurrence to date; and the long follow-up on some of these is noteworthy.

A review of the published cases of tumors found at autopsy, and considered possibly malignant, is given in Table V. It is noteworthy that in neither

TABLE V

HYPOGLYCEMIA. ISLET CELL TUMORS FOUND AT AUTOPSY. SUSPECTED OF BEING MALIGNANT—THREE CASES

Author	Date	Single or Multiple	Capsule Microscopically	Blood Vessel Invasion	Insulin Extracted	Autopsy
1. Thalhimer and Murphy[76]	1928	Single	Incomplete	Not described	0	No metastases
2. Moersch and Kernohan[57]	1938	Single	Incomplete	Not described	0	No metastases. Degenerative changes in brain

TABLE VI

SUMMARY OF THE STATISTICS IN TABLES I, II, III, IV AND V

Islet Cell Tumors with Hypoglycemia

	No. of Cases*	
Tumors removed at operation and considered benign	46	
Tumors found at autopsy and considered benign	24	
Total benign tumors		70
Tumors removed at operation and suspected malignant	19	
Tumors found at autopsy and suspected malignant	2	
Total suspicious tumors		21
Carcinoma with metastases, proved malignancy	5	5
Total islet cell tumors	96	96

* These statistics represent individual cases and do not include the number of multiple tumors found in some instances.

Pathology

Benign Cases:*

Capsule: Complete	28	Blood vessel invasion: Stated absent	15
Incomplete	20	Not described	55
Not described	22		70
	70		

* In these benign tumors there are reports of successful specific staining of the granules in the tumor cells 11 times. Insulin extractions of the tumors were done successfully eight times. These procedures were undertaken only on the operative material, except for one insulin extraction.

Questionable Cases:*

Capsule: Complete	1	Blood vessel invasion: Present	7
Incomplete	15	Stated absent	1
Not described	5	Not described	13
	21		21

* In these questionable cases there are reports of successful specific staining of the granules in the tumor cells four times, and successful insulin extraction once. All these were in operative material.

Proved Cases:*

Capsule: Probably not complete in any case—5 cases

Blood vessel invasion: Not described—5 cases

* Sites of metastases: Liver, lymph nodes, mesentery, peritoneum and epicardium.

of these were metastases found. Also of interest in this table and Table III are the occurrence of changes in other endocrine glands, and the changes in the central nervous system, which confirm the clinical impression of the possibility of persistent mental deterioration in prolonged untreated cases.

It seems improbable that all of the tumors with histologic suggestion of carcinoma were really such, as the proportion of these to the benign tumors is so high, 21 to 70, and the follow-up in some cases is so long. It would be gratifying to feel that surgery had eliminated malignant disease in all these cases. But, of these suspected tumors, are there some in which blood vessel invasion, demonstrated, means that metastases, not demonstrable, were present at the time of removal of the primary growth, and will these eventually develop symptoms of hyperinsulinism?

If one wishes to consider the so-called "adenoma malignum" type of carcinoma of the thyroid as possibly analogous to these well-differentiated islet cell tumors with blood vessel invasion, then it might be that, like the thyroid tumors of this type, distant metastases might be late and slow. But the metastasizing tumors of the thyroid do not give evidence of their presence by hyperthyroidism, and it is conceivable that even in small metastatic foci of islet cell tumors hypoglycemia might occur early. Thus far no reported case has illustrated this, but it seems a good possibility. How long one should wait to feel secure about such functional metastases, and whether one can predicate that symptoms should appear early, is pure speculation. It will be of the utmost importance to follow all of these patients with these rare tumors for many years, and in the event of recurrence, or metastases after apparently successful removal, to publish such findings so that clinician and pathologist will have some basis for prognosis.

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ACUTE PANCREATITIS AND DIABETES

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DURING the past year I have had the opportunity to thoroughly study a patient, known to have been free of diabetes previously, who developed severe persistent diabetes mellitus during convalescence from acute hemorrhagic pancreatitis. A cursory survey of the literature revealed a wide diversity of opinion concerning the rôle of acute pancreatitis in the production of diabetes. On the one hand, the incidence of diabetes as a sequela was not only obviously rare, but most authors writing on acute pancreatitis had neglected to note it as a possibility or had merely mentioned it in passing. On the other hand, certain investigators interested in metabolic diseases have expressed the view that even mild, unrecognized attacks of pancreatitis may be an important factor in causing diabetes or in bringing about exacerbations of preexisting diabetes. This divergence of thought has made it advisable to restudy the problem. I shall first report in some detail my own case; secondly, summarize the pertinent data from a series of cases of severe pancreatitis from the New Haven Hospital; and finally, review the literature.

Case Report.—T. M., male, age 27, was admitted to the New Haven Hospital, February 17, 1938, complaining of severe epigastric pain. There had been no diabetes in the family. The past history was irrelevant except for occasional bouts of drinking. There was nothing suggesting diabetes, no polyphagia, polydipsia, polyuria, or weight loss. He had been previously admitted, late in 1934, with a gonococcal urethritis, prostatitis, and arthritis. Five weeks before admission he had been confined to another hospital in the city with a brief attack of right lower quadrant pain. His urine had never shown sugar. In general he had been quite well. For a week he had had anorexia and occasional mild epigastric postprandial discomfort. Three days before admission he had a stool which he described as "black."

The present illness began at 8 A.M. on the morning of February 17, when he was suddenly seized with excruciating epigastric pain which "bore through" to his back and which persisted. He began to vomit almost immediately and continued to vomit frequently. There was no gross blood in the vomitus. At noon and again at 10:30 P.M. his physician gave him a hypodermic of morphine. Finally, at midnight he was sent to the hospital.

Physical Examination.—Temperature 100.6° F., pulse 86, respirations 24, blood pressure 120/76. He appeared to be in agonizing pain and was obviously very ill, sweating profusely, vomiting frequently. The abdomen moved little with respiration, was board-like in the epigastrium, less spastic in the lower quadrants, and extremely tender all over, but especially in the midepigastrium. There was generalized rebound tenderness. There was no distention, no shifting dulness. There was no obliteration of liver dulness. The examination was otherwise not remarkable. The blood examination showed: Erythrocytes 5,400,000; hemoglobin 100 per cent; leukocytes 16,000, 96 per cent neutrophils and 32 per cent nonsegmented forms. The urine examination: Specific gravity

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1.034, acid, albumin 2 plus, sugar negative, acetone 2 plus, rare white cells. It was the impression that the patient had a perforated peptic ulcer.

On the way to the operating room roentgenograms were taken which were negative for pneumoperitoneum. A Wangensteen stomach suction was instituted. While waiting, at the patient's request, for a priest to arrive, the pulse began to rise and blood pressure to fall, and in spite of an infusion of glucose and saline his pulse had risen to 160 and his systolic pressure had dropped to 60 by the time the operation was begun.

Operation.—Under ether and venethene anesthesia supplemented with local infiltration, the peritoneal cavity was entered through a small upper right rectus incision and a large amount of "tomato soup" fluid was immediately encountered. There were extensive and marked fat necroses. There was a mass in the region of the pancreas, some omental adhesions over the duodenum, and no evidence of ulcer. Through the foramen of Winslow was emitted much dark blood-stained fluid. The lesser sac was entered through the gastrocolic ligament. The pancreas was about twice the normal size, the head being somewhat more enlarged than the body and tail. The entire organ was soft, necrotic, and discolored with ecchymoses. Two Penrose drains were inserted, one toward the head of the pancreas, the other toward the tail. The gallbladder and the common duct appeared and felt normal. A cholecystostomy was performed and the wound closed. By the end of the procedure the patient had received 1,900 cc. of glucose and saline solution and the blood pressure had risen to 100/50. A transfusion of 500 cc. of citrated blood was given. The blood pressure was now 125/68 and the pulse 110.

The patient did well. His temperature rose on the first day to 102.8° F., but fell promptly, and ranged between 99° and 100.5° F. for the next five days, after which it was normal. For a few days he was somewhat delirious. The wound drained profusely for 24 hours, but little thereafter. The drain was removed on the eighth day. A lipiodol visualization of the biliary tract on March 1, 1938, showed normal gallbladder and cystic and common ducts. The following day the catheter was removed, and two days later the wound was closed and an intravenous cholecystogram was made. This showed nonvisualization, which was interpreted as a postoperative effect. A liver function test (tetra-iodo-phenolphthalein) revealed 5 per cent retention in 30 minutes.

The admission urine had been negative for sugar. After operation and infusion there was complete reduction of Benedict's solution and only a trace of acetone. Glycosuria persisted. When he was put on a measured diet (P. 70, F. 150, C. 150) on February 25 most of the fractional specimens were showing complete reduction. He improved somewhat, and when he was finally discharged, March 6, 1938, he was only occasionally excreting sugar on a diet of P. 80, F. 175, C. 200. The blood sugar had been 111 mg. per cent on February 22. It was 104 on February 26, and a glucose tolerance test revealed a fall to only 157 in two hours. This was repeated on March 1. The fasting value was 124; it rose to 214 in one hour; and was 191 in two hours.

On return to the clinic, March 9, 1938, he was weak and thirsty and had polyuria and mild abdominal discomfort. The urine showed complete reduction of Benedict's solution, but no acetone.

He was readmitted, May 30, 1938, complaining of excessive hunger, thirst, and polyuria. He had not adhered to his diet. He said that he had been drinking six to eight quarts of milk, three to four quarts of water, and ten bottles of beer a day. He had been to the clinic only once, to his family doctor once, and had tested his urine himself only three times. On all occasions, it showed complete reduction. He had had marked polyuria, cramps in his calves the past few nights, and some constipation. He had had mild epigastric pain about twice a week for which, in spite of advice to the contrary, he had taken beer. He had lost about 20 pounds. He was definitely acidotic. Fractional specimens of urine showed complete reduction of sugar and from

2 to 4 plus acetone. He was immediately started on insulin therapy and after 48 hours the acetone disappeared from the urine for the most part. Insulin was rapidly increased from 30 units a day to a maximum of 110 units on June 8, when for the first time he became relatively free of glycosuria. He was now on a diet of P. 100, F. 250, C. 300, and was constantly complaining of hunger. He was discharged, June 14, on this diet, with 55 units before breakfast and 30 units before supper, on which regimen he was moderately well regulated. On May 31 the blood sugar was 158 and cholesterol 450. On June 8 the blood sugar was 219. A bromsulphalein liver function test showed no retention in 40 minutes; intravenous cholecystograms showed poor filling but prompt emptying after a fatty meal, probably due to his recent cholecystostomy. He had gained ten pounds and now weighed 152.

He was readmitted, August 27, 1938, with an attack of abdominal pain similar to but less severe than his original one, and it was felt that he might be suffering from a mild recurrence of pancreatitis. This attack cleared up under conservative therapy. He had not followed his diet or taken his insulin for a month and had indulged in bouts of drinking. His diabetes was finally regulated on a diet of P. 90, F. 200, C. 200 with 30 units before breakfast and 15 units before supper. Liver function test again showed no retention of dye. Blood sugar was 182 mg. per cent on September 6. On discharge, September 13, he weighed 156 pounds.

On November 17, 1938, he was again sent into the hospital for regulation. He had taken his insulin (except occasionally when drunk), his urine had recently showed a "brick-red" test, he was constantly hungry and thirsty, and he was drinking about nine quarts of milk a day and soda pop "incessantly." He had polyuria, weakness, and fatigability. For two weeks he had had a "cold in the chest" and was producing about a cup of foul sputum a day. He had a diffuse rash. Kahn and Wassermann reactions were positive. The urine showed complete reduction of Benedict's solution and much acetone. A diagnosis of secondary syphilis and pyogenic right upper lobe abscess was established. The former was treated with bismuth and mepharsen, the latter by postural and bronchoscopic drainage. The abscess resolved. He was discharged, December 30, 1938, on a diet of P. 90, F. 250, C. 175 with 30 units of insulin before breakfast and 15 units before supper.

Three days later he was seen again with a respiratory infection. At this time he had marked glycosuria, and his insulin was increased to 30-0-30. The following day there was again glycosuria and acetonuria, and hospitalization was advised. He went to another hospital where he remained for three weeks. Since then he has continued with antileutic therapy. His diabetes remains exceedingly difficult to regulate.*

NEW HAVEN HOSPITAL SERIES

The case just presented is the only instance in the New Haven Hospital in which diabetes has developed as a complication or sequela of acute pancreatitis. During the past 17 years there have been 18 cases of severe acute hemorrhagic pancreatitis. The pertinent data are recorded in Table I. Mild cases of pancreatitis and suspected cases not proved by operation or autopsy are excluded. The patients varied in age from 24 to 68 years; six were males, 12 females. All except one were subjected to operation. Six of 17 patients treated by operation died, a mortality of 35 per cent. Case 7 was known to have diabetes. Excluding this case, four, or 27 per cent, showed glycosuria

* Since submission of this paper for publication the diabetes of the patient, T. M., has remained severe. He was admitted in a diabetic coma in September, 1939. He now requires about 75 units of insulin daily. Following the lung abscess he developed bronchiectasis in the right upper lobe, and in November, 1939, he was found to have contralateral apical tuberculosis with cavitation. He is now under treatment for this in a Sanitarium.

at some time during the acute illness, though only one (6 per cent) had glycosuria on admission. Two of the four patients with glycosuria died. Three patients upon whom blood sugar determinations were made showed some elevation.* Only one patient developed diabetes. Careful follow-up studies are not available, although several patients seen at varying intervals after operation were in apparent good health. A few of the cases are of some particular interest.

TABLE I

CASES OF SEVERE ACUTE HEMORRHAGIC PANCREATITIS IN THE NEW HAVEN HOSPITAL

No.	Year	Name	Age	Sex	Diagnosis Established By		Glycosuria		Blood Sugar	Outcome	Remarks
					Operation	Autopsy	On Admission	Subsequently			
1	1921	M. W.	48	F.	Yes	No	No	No	..	Died	Urine negative 5 mos. later
2	1923	A. H.	59	F.	Yes	No	No	No	..	Recovered	
3	1923	N. H.	47	F.	Yes	No	No	No	..	Recovered	
4	1923	E. H.	52	F.	Yes	No	No	No	..	Recovered	
5	1924	J. B.	56	M.	Yes	No	No	No	..	Recovered	
6	1925	J. M.	62	M.	Yes	No	No	No	..	Recovered	
7	1926	H. K.	68	F.	No	Yes	Yes	Yes	469	Died	Known diabetic for 5 yrs. (see text)
8	1928	I. E.	29	F.	Yes	No	No	No	..	Recovered	
9	1930	E. G.	32	M.	Yes	No	No	No	..	Recovered	Questionable recurrence 3½ yrs later. Urine negative
10	1931	P. H.	36	F.	Yes	No	No	No	..	Recovered	
11	1932	O. S.	63	M.	Yes	No	No	No	..	Died	
12	1932	M. B.	31	F.	Yes	No	No	No	..	Recovered	
13	1934	C. C.	48	F.	Yes	No	No	Yes	155	Died	See text
14	1936	E. R.	45	F.	Yes	No	Yes	..	..	Died	
15	1936	H. S.	45	F.	Yes	Yes	No	No	..	Died	
16	1936	G. H.	30	M.	Yes	Yes	No	No	..	Died	
17	1938	T. M.	27	M.	Yes	No	No	Yes	124	Recovered	Diabetes developed (see text)
18	1938	M. D.	24	F.	Yes	No	No	Yes	150	Recovered	Urine negative 8 mos. later (see text)

ILLUSTRATIVE CASE REPORTS

Case 7.—This 68-year-old female was admitted in coma. A diagnosis of mild diabetes had been established five years previously. No glycosuria had been observed when she was seen at intervals after that time. Five days before admission she caught cold and glycosuria appeared. It increased as the upper respiratory infection became worse, but three days before admission she was practically well. Frequency and polydipsia began and she became stuporous 24 hours before admission. She was brought to the hospital in coma. There was upper abdominal tenderness and the diagnosis of acute pancreatitis was considered. In spite of intensive therapy, the coma persisted and she died within a few hours. At autopsy acute hemorrhagic pancreatitis and cholelithiasis with calculi in the common duct and in the duct of Wirsung were found.

This case is instructive from two points of view: First, as an example of how disastrous acute pancreatitis may be in a patient with relatively mild diabetes; and secondly, how hazardous it is to attribute diabetic coma in

* Normal values in the New Haven Hospital range from 55 to 75 mg. per cent.

acute pancreatitis to the latter process alone unless the patient is known not to have been a diabetic previously.

Case 13.—This 48-year-old woman was admitted with acute pancreatitis of nine hours' duration. She had had a previous admission for acute cholelithiasis, at which time the urine was sugar free. The urine on this admission contained albumin and acetone, but no sugar. A postoperative sample of blood showed a sugar of 155 and N.P.N. of 42. The next morning, several hours after an infusion of glucose and saline, the blood sugar was 251, the N.P.N. 47. The patient had received some morphine. She failed to respond. The first impression was that she was in a diabetic coma. There was an acetone breath. The blood pressure was 92/50. She was given blood, glucose and saline intravenously, and insulin. An hour and a half later she responded. The urine during this period showed complete reduction and 1 plus acetone. Four hours after the last dose of insulin the blood sugar was 76. The next day it was 62 and she was given no insulin. She had signs of pneumonia. She was given a little insulin off and on, but had no further glycosuria. She developed a pneumococcus septicemia and died after seven days in spite of repeated transfusions and other supportive measures.

This patient undoubtedly had some disturbance of carbohydrate metabolism, though it is, at least, to be questioned whether her period of coma was really due to hyperglycemia and acidosis.

Case 18.—This patient was a 24-year-old woman who had had several attacks suggesting acute cholecystitis. She was admitted in an attack differing from the others in that there was a great deal of left upper quadrant as well as right upper quadrant pain. There were signs of diffuse peritoneal irritation. At celiotomy, acute hemorrhagic pancreatitis and chronic cholecystitis with cholelithiasis were found. The lesser sac was drained and a cholecystostomy performed. During convalescence she sloughed considerable quantities of pancreatic tissue. There was no glycosuria on admission, but complete reduction following operation and again the next day after an infusion of glucose. The following day the sugar was 1 plus, and on several occasions during the week there was a trace of sugar in the urine. There were never acetone bodies. The blood sugar was slightly elevated on several occasions, 107 to 150 mg. per cent. A glucose tolerance test on the twenty-fourth postoperative day revealed values of 150, 282, 216, 112 and 104 (fasting, one-fourth, one-half, one and one-half and two hours) and on the fortieth postoperative day values of 98, 199, 125, 99 and 93 mg. per cent (fasting, one-fourth, one-half, one and two hours). Her family doctor writes that her health has remained good and that her urine was normal when last examined, nine months after operation. This patient had a mild transient interference with carbohydrate metabolism.

Although my concern has been primarily with the association of true diabetes mellitus and acute pancreatitis and not with those transient manifestations of disturbed carbohydrate metabolism which are occasionally observed during the course of acute pancreatitis, it will be advisable to consider the latter briefly since they may shed some light upon the former.

Glycosuria.—In Reginald Fitz's original communications[1, 2] on acute pancreatitis the occurrence of glycosuria is not mentioned. In 1895, Atkinson[3] reported a fatal case of gangrenous pancreatitis with slight glycosuria. Thirty years earlier, Harley[4] had reported a case of long-standing obstruction of the pancreatic and common bile ducts with pancreatic abscess in which there was terminal glycosuria. Six of the 44 instances of acute pancreatitis described by Körte[5] were associated with glycosuria. Most authors since then have noted this in approximately the same percentage of cases—Egdahl[6] in 5 per

cent, Guleke[7] in 10 per cent, Sebening[8] in 10 per cent, Bernhard[9] in 12 per cent, and Mahner[10] in 10 per cent. All are agreed that glycosuria is found in such a small proportion of patients, and is not always found, even then, on the first examination, as to make it of little help in the differential diagnosis.

In 1927, Schmieden and Sebening[11, 12] presented a study of 1,278 operatively treated cases of acute pancreatitis collected from the literature and from personal communications in the postwar period. To these I have added, in Table II, an additional 1,600 cases, gathered from the literature, since the time of their report.* Data are available on about 700 of these in which glycosuria occurred about 78 times, or approximately 11 per cent.

Hyperglycemia.—In 1924, Calzavara[87] reported that, in experimentally induced acute pancreatitis in dogs, hyperglycemia was an early and constant finding, reaching a maximum in six hours (often ten times the normal value) and persisting to death. If the pancreas was drained the blood sugar gradually fell. There was no glycosuria. He ventured to suggest that this observation might be found clinically and be of considerable diagnostic importance. Douglas,[71] among others, states that blood sugar determinations have not proved to be of any great value in the early diagnosis of acute pancreatitis, and Fiessinger[88] says that hyperglycemia is as inconstant as is glycosuria. Others,[25, 81, 89 to 96] however, claim that hyperglycemia occurs very frequently and is of considerable diagnostic aid. Although he had only a few determinations, Brocq[97] suggested, in 1926, that if hyperglycemia should be found with any regularity it might prove of great importance for diagnosis and prognosis. Later, he and Varangot[81] collected from the literature 72 cases in which blood sugar determinations were available, and of these 15 had values of less than 150, 23 from 150 to 200, and 34 over 200 mg. per cent. Gabrielle[92] states that hyperglycemia is a constant finding, and Bernhard[89] points out that the blood sugar may be normal in mild cases though it is elevated in most severe cases of acute pancreatic necrosis. Wildegans[93, 94] agrees with the latter opinion, but states that there is hyperglycemia in all severe cases and that this determination is of prime diagnostic value. Because other acute abdominal diseases may occasionally be associated with a mild hyperglycemia, it has been suggested[81, 84] that only values of 200 mg. per cent or more be considered of diagnostic importance. Perhaps, because of the varying normal values with different technics, it should be considered of significance if the blood sugar is elevated to about twice the normal level.

In Table II data are available in 55 cases. Of these, 28 patients, or 50 per cent, had blood sugars of 200 or more, nine (18 per cent) between 150 and 200, and six additional cases showed slight elevation (125 to 150 mg. per cent). In addition, Kerschner[23] states that there were four patients with hyperglycemia in a series of 41 cases without stating the number upon whom determinations were made. The question arises whether the relatively high

* An attempt has been made to limit the selection of cases to those of relatively severe acute pancreatitis, proved by operation or autopsy, and this has been done except in a few instances where reports have included a small number of cases not so proven.

TABLE II

CHANGES IN CARBOHYDRATE METABOLISM IN AND FOLLOWING ACUTE PANCREATITIS

Author	No. of Cases	No. Surviving	No. With Glycosuria	No. With Hyperglycemia	No. Followed by Disturbed Glucose Tolerance But Not True Diabetes	No. Followed by Diabetes	Remarks
Schmieden and Sebening[11] (1927)	1,278	624	..	..	..	18	
Brütt[13] (1927)	33	20	..	..	*	1†	* Most cases studied soon after acute illness. † See Table V
Von Redwitz[14] (1927)	1	1	..	0	..	1*	* See Table V
Kummer[15] (1927)	8	3	2	..	..	..	
Warfield[16] (1927)	2	0	2	1	..	2*	* See Table V
Watkins[17] (1928)	18	8	2	1*	..	..	* Another had blood sugar of 150 mg. %
Delmore[18] (1928)	13	11	..	..	..	..	
Kreiner[19] (1928)	2	1	1	1*	..	0	* Another had blood sugar 21% above normal
Grant[20] (1928)	12	5	2	..	..	..	
Ney[21] (1929)	28	28	3	1	3	5*	13 of the 28 were examined in follow-up studies. * See Tables IV and V
Walzel[22] (1929)	40	20	..	1	..	2*	* Cleared up after drainage of pseudocysts
Kerschner[23] (1929)	41	12	Few	4	..	2*	* See Table III
Tammann[24] (1929)	38	18	..	..	6*	0	* 12 cases studied
Jorns[25] (1929)	18	18	Few	6	5*	1†	* 7 cases studied. † See Table V
Linder and Morse[26] (1929)	88	65	..	..	..	..	
Olds[27] (1929)	7	5	0	1	..	..	
Simon[28] (1929)	6	1	..	..	..	..	
Kramer[29] (1920)	7	4	0	..	..	..	
Cullen and Friedenwald[30] (1929)	4	1	2*	..	..	*	* One case of preexisting diabetes
Oehler[31] (1929)	26	11	0	..	..	..	
Warren[32] (1930)	6	0	..	..	..	6*	* See Table III
Eliason and North[33] (1930)	14	7	1	..	..	..	
Bayer[34] (1930)	1	0	1	1	..	1*	Died in coma. * See Table III
Weeden[35] (1930)	12	4	..	..	..	..	
Stocker[36] (1930)	36	15	..	..	..	..	
Matthaes[37] (1931)	21	21	..	..	2	1*	* See Table III
Bernhard[38] (1931)	75	50	9	..	5*	5†	* 25 cases studied. † See Tables III and V
Hopkins[39] (1931)	1	1	0	..	..	0	
Dunn[40] (1931)	1	0	1	..	..	0	
Mackechnie and Olsen[41] (1931)	1	1	0	0	*	0	* Blood sugar 134 about a month after operation
Grant[42] (1931)	4	1	..	2	..	..	
Unger and Sostmann[43] (1931)	100	54	..	..	5*	1†	* 16 cases studied. † Another case of preexisting diabetes. See Table V
Kappis[44] (1931)	75	38	..	..	..	..	
Martens[45] (1931)	122	68	12	..	..	1*	* See Table V
Rich[46] (1932)	6	4	1	0	..	..	
Felsenreich[47] (1932)	32	11	4	..	..	1*	* Another known diabetic died in coma. See Table IV
McWhorter[48] (1932)	64	29	8*	..	..	1†	* 5 of these died. † See Table V
deTakats and MacKenzie[49] (1932)	30	19	4	*	2†	2‡	* 2 showed mild hyperglycemia, one an altered glucose tolerance curve on fifth p.o. day. † 4 studied. ‡ See Table V
Jones[50] (1932)	1	1	..	*	..	0	* Blood sugar was 140 mg. %

TABLE II (*Continued*)

Author	No. of Cases	No. Surviving	No. With Glycosuria	No. With Hyperglycemia	No. Followed by Disturbed Glucose Tolerance But Not True Diabetes	No. Followed by Diabetes	Remarks
Lyall[51] (1932)	3	0	..	..	..	..	
Quick[52] (1932) / Downie[53] (1932)	49	22	3	..	2	1	11 cases studied. See Table V
Lemieux[54] (1932)	1	1	..	..	..	1*	* See Table V
Truesdale[55] (1932)	54	43	..	..	..	*	* One patient died in coma, presumably a preexisting diabetic
Haynes[56] (1933)	6	5	..	..	..	..	
Hartlieb[57] (1933)	27	13	..	..	..	..	
Jacobovici[58] (1933)	14	8	2*	1	..	*	* A patient with preexisting diabetes
Thomas[59] (1933)	3	2	0	..	..	..	
Finney[60] (1933)	32	20	..	..	..	..	This includes the cases reported by Rienhoff and Lewis[61]
Koster and Kasman[62] (1934)	22	17	2	..	..	..	
Horine[63] (1934)	13	7	1	0	..	..	
Harve[64] (1935)	11	9	..	..	1	..	
Donald[65] (1935)	6	4	1	..	..	..	
LeSage and LeSage[66] (1935)	4	4	0	..	..	..	
Henderson and King[67] (1935)	60	28	4	..	..	..	
Dobbs[68] (1935)	15	6	1	..	..	..	All cases of acute pancreatitis in children
Huet[69] (1935)	1	1	..	..	..	..	
Douglas[70] (1933) / Douglas[71] (1935)	38	20	..	..	..	*	* One patient died in coma, presumably an old diabetic
Mendelssohn[72] (1936)	6	3	0	..	..	..	
deKlimko[73] (1936)	19	8	..	..	3*	0	* 6 cases studied
Rochet[74] (1936)	6	3	..	..	..	..	
Mahner[10] (1937)	19	13	3	..	..	..	
Joslin[75] (1937) / Jurist[76] (1909)	1	1	0	..	..	1*	* See Table V
Weir[77] (1937)	47	..	3	..	..	..	
Gatewood[78] (1937)	2	2	0	..	..	..	
Sedgley[79] (1937)	2	2	0	..	..	0	
Trasoff and Scarf[80] (1937)	16	4	..	10*	..	..	* All 10 cases studied had values of 190 mg. %—or more
Brocq and Varangot[81] (1937)	1	1	1	1	..	1	A case of temporary diabetes
Kufferath and Volkmann[82] (1938)	65	44	..	..	..	..	
Beck[83] (1938)	10	2	1	3	..	*	* One patient with a history of glycosuria for 10 mos. died in coma
Dunlop and Hunt[84] (1938) / Hunt[85] (1928)	11	7	2	6*	..	..	* Only 6 cases studied
Abell[86] (1938)	30	21	..	..	..	..	

percentage of patients with elevation of blood sugar is due to omission from published reports of normal values. It may be said, however, that individual reports are in agreement. For example, Jorns[25] found hyperglycemia in all of eight patients studied (three over 200, four over 150 mg. per cent); Trasoff and Scarf[80] in all of ten patients studied (all over 190 mg. per cent); and Dunlop and Hunt[84] in all of six patients studied (five over 200 mg. per cent).

Bernhard[89, 98] feels that a glucose tolerance test is of greater diagnostic aid than is fasting blood sugar estimation. He states that mild cases of acute pancreatitis in which there may be no hyperglycemia are likely to show an abnormal glucose tolerance curve. Furthermore, he states that, though

other acute abdominal conditions, *e.g.*, empyema of the gallbladder, may occasionally manifest hyperglycemia, they do not show the changes in glucose tolerance which he considers characteristic of acute pancreatitis. There are few instances in the literature in which this test has been recorded, but where it has been used it has apparently borne out his observation. Mikkelsen[99] agrees that this is a more helpful procedure in diagnosis than blood sugar determination, and Wildegans,[94] likewise, feels that in mild cases of pancreatitis it is of greater assistance. Troissier, Bariety, and Gabriel[100] have recorded an unusual case with a reversed hyperglycemia glucose tolerance curve.

A number of authors[9, 66, 101] have suggested that the occurrence of marked glycosuria, or more especially of hyperglycemia, may be a bad prognostic sign. Certainly, many examples may be cited in support of this opinion in addition to the fatal cases of true diabetes which will be discussed subsequently. Neumann[102] had a patient who was admitted on the second day of his illness with 6.5 per cent sugar in the urine and acetone breath, who died the day after operation. Dunn[40] lost a patient whose urine was loaded with sugar within 29 hours of the onset of symptoms. Bernhard[9] had a fatal case in which the blood sugar rose in 18 hours from 260 to 370 mg. per cent. Dunlop and Hunt,[84] likewise, reported a case in which the blood sugar rose from 210 on the first postoperative day to 360 mg. per cent before death, on the fifth day. One of Grant's[42] fatal cases had a blood sugar of 400 mg. per cent. Geinitz[103] lost a patient who had glycosuria and a blood sugar of 341 mg. per cent in spite of the use of insulin. Walzel[22] had a patient with a sugar of 340 mg. per cent 12 hours after operation who died in 36 hours in spite of insulin therapy. Whipple and Speese[101] describe the case of a patient whose blood sugar was 384 mg. per cent the day after operation. Insulin failed to control the blood sugar after two weeks, and the patient died within four weeks. There was only slight glycosuria on a few occasions and never acetonuria. On the other hand, many instances might be presented in which there has been marked hyperglycemia and recovery. Of the 28 patients listed in Table II with blood sugar values in excess of 200 mg. per cent, 14, or 50 per cent, died—about the mortality rate of the entire group of cases.

Diabetes Mellitus.—Having thus established the fact that disturbances of carbohydrate metabolism of greater or less degree occur in a rather high percentage of patients with acute pancreatitis, I shall now consider true diabetes mellitus during the course of and following this disease. Although most text-books on surgery do not mention diabetes as a complication or sequela, such cases have appeared from time to time in the literature since the latter part of the nineteenth century. An attempt has been made to review all of these.

In Table II it will be seen that, excluding those cases of known preexisting diabetes, this affection as a permanent disease follows 52 times in a series of some 2,855 cases of acute pancreatitis, an incidence of about 2 per cent. The fact that a certain number of these cases are reported, particularly because of the diabetes, is perhaps offset by cases which have not

TABLE

CASES OF DIABETES BEGINNING

Author	Diagnosis	Sex	Age	Operation	Autopsy
					CASES OF DEATH
Benda and Stadelmann[104] (1896)	Acute pancreatitis	F.	23	No	Yes
Neumann[102] (1904)	Acute hemorrhagic pancreatitis with almost total necrosis	F.	24	Yes	Yes
Holten[105] (1924)	Acute necrosis (total) of pancreas	F.	48	No	Yes
Rodriquez[106] (1924)	Acute pancreatitis	M.	59	No	Yes
Tscherning[107] (1925)	Hemorrhagic pancreatitis with severe necrosis	F.	31	No	Yes
Bayer[24] (1930)	Acute pancreatic necrosis	M.	28	No	Yes
					OTHER CASES OF DEATH
Franke[108] (1902)	Acute hemorrhagic pancreatitis	M.	42	No	Yes
Bosanquet[109] (1905)	Acute hemorrhagic pancreatitis	F.	53	No	Yes
Caro and Winkler[110] (1918)	Acute hemorrhagic pancreatitis	M.	..	No	Yes
Warfield[16] (1927)	Acute hemorrhagic pancreatitis	M.	69	Yes	No
Warfield[16] (1927)	Acute pancreatic necrosis	M.	50	Yes	Yes
Kerschner[23] (1929)	Acute pancreatitic necrosis	..	..	Yes	..
Kerschner[23] (1929)	Acute pancreatic necrosis	..	..	Yes	..
Warren[22] (1930)	Acute pancreatitis	6 cases		?	Yes
					CASES WITH SURVIVAL
Brentano[111] (1902)	Acute pancreatitis with subsequent subphrenic abscess	F.	24	Yes	No
Peisner[112] (1902)	Acute pancreatitis and hemorrhagic pseudocyst	F.	28	Yes	No
Albu[113] (1911)	Acute pancreatitis with abscess	F.	29	Yes	No
Vogel[114] (1924)	Acute pancreatitis	..	..	Yes	No
Matthaes[27] (1931)	Acute pancreatitis with abscess	F.	..	Yes	No
Bernhard[28] (1931)	Acute pancreatic necrosis; subtotal infarct	..	32	Yes	No

been diagnosed either because of lack of interest or of systematic follow-up studies. In addition, some 10 similar cases have been collected from the earlier literature. Since I have found, during the period covered by Schmieden and Sebening's[11] report, only ten cases, it is apparent that eight of the 18 mentioned by these authors were collected through personal communications, or have failed to come to my attention in the literature. Altogether, then, there are some 62 cases of diabetes thought to be etiologically related to acute pancreatitis. The available data on these are assembled in Tables III, IV and V. Only cases in which the diagnosis was established at celiotomy or autopsy are included. Other more doubtful cases will be referred to subsequently.

III

DURING ACUTE PANCREATITIS

Onset of Diabetes	Character of Diabetes	Remarks
IN DIABETIC COMA		
On admission	Died in coma after 1 wk.	Was entirely well without symptoms of diabetes before acute illness
On admission	Died on tenth p.o. day, 1 day in coma	No definite proof of no preexisting diabetes, though, presumably, there was none. Treated unsuccessfully with diet and soda bicarb.
On admission	Died on third day of illness, in coma	Urine negative 5 wks. before. Insulin therapy
On admission	Died in 2 wks., in coma	Urine negative 6 wks. before. Insulin therapy
Within 2 wks.	Died in coma, 6 days after adm.	Urine negative 16 days before death. Insulin therapy
Within 1 wk.	Died in coma in 2 wks.	Never any diabetic symptoms before. Insulin therapy
DURING ACUTE ILLNESS		
With onset of P.-I.*	Fulminating	Died 2 wks. Never any symptoms of diabetes before P.-I.*
With onset of P.-I.*	Severe	Died in collapse with acidosis but without coma within 2 wks.
On admission	Severe	Died within a few days. Acidosis. Urine negative during attack. Questionable cholecystitis 1 yr. before
On admission	Severe	Operation on twelfth day. Death. Presumably not a diabetic previously
Semicoma with onset of pain	Severe	Operation 1 mo. after onset of P.-I.* Death in 10 days. Had recently been examined and nothing abnormal found
....	Severe	Died on fifteenth p.o. day
....	Severe	Died on third p.o. day
"After the onset of symptoms"	....	No other details
*P.-I. represents "present illness."		
OF ACUTE ILLNESS		
11 days p.o., 6 wks. after onset	Regulated with diet	Glycosuria decreased with diet; recurred again on mixed diet Large sequestrum (12x4x½ cm.)
Within 2 wks.	Died in coma in 6 mos.	Apparently no diabetes 2½ wks. before, during delivery. Diet and soba bicarb. Sequestrum (19x7x3 cm.)
In 1 wk.	Severe with acidosis	Urine negative on admission. Followed for 2 yrs.
....	....	Diabetes did not exist before. No other details
During acute illness	Fairly severe	Followed for 4 yrs. Under constant supervision
Within 2 wks.	Died in 4 yrs. in coma	Passed small sequestra after operation

In Table III are listed 25 cases of diabetes beginning during the course of acute pancreatitis. Six of these patients died within a short period in diabetic coma. A number were treated with insulin. Thirteen died during the acute illness with severe diabetes, though apparently not in coma. No information concerning six of these[32] is available. Six patients whose diabetes began during the acute pancreatitis survived the acute illness. Two of the six[38, 112] died later in coma (six months and four years, respectively). Brentano's[111] patient had not been followed long at the time of his report but apparently had a mild diabetes. No details are given in Vogel's[114] case. The other two patients[37, 113] were followed for two and four years, respectively, and had severe diabetes. It should be mentioned that sequestration of the

pancreas was noted in three of these six patients who survived their acute illness.

TABLE IV

CASES OF DIABETES BEGINNING SOON AFTER ACUTE PANCREATITIS

Author	Diagnosis	Sex	Age	Operation	Autopsy	Onset of Diabetes	Character of Diabetes	Remarks
Umber[115] (1925)	Severe acute pancreatitis. Necrosis	F.	27	Yes	No	1½ mos. after operation	Managed well on insulin	Large sequestrum—almost all of pancreas. Pt. followed 2 yrs.
Orthner[116] (1925)	Entirely infarcted hemorrhage pancreas	F.	28	Yes	No	Soon after discharge (discharged in 8 wks.)	Managed well on insulin	Large sequestrum passed on sixteenth p.o. day
Ney[21] (1929)	Lesser sac abscess from pancreatitis; cholecystitis; cholelithiasis	F.	37	Yes	No	3 mos. after operation	Mild	Urine neg. on adm. Transient glycosuria postoperatively
Felsenreich[47] (1932)	Acute pancreatic necrosis. Total infarct	F.	36	Yes	No	....	Severe	No sequestrum

In Table IV are grouped four cases of diabetes with onset within a short period after recovery from acute pancreatitis. One patient had a mild diabetes,[21] one a severe case,[47] two were managed well on insulin.[115, 116] Two of the four had extensive sequestration of the pancreas.

In Table V are listed those cases of diabetes which ensued a year or more after acute pancreatitis and also a few in which the exact time relationship is not available. Altogether, there are 33 cases in which the diabetes came on from one to 22 years after the acute illness—an average of about seven years. In all the cases the pancreatitis was relatively severe; considerable sequestration was noted in four; and a long, persisting fistula in three instances. Six patients died with severe diabetes;[21, 38, 45, 75, 111] no data are available as to the severity in 13 cases; four patients had mild diabetes; the remainder more or less severe.

It may be pointed out that practically all of the 62 patients listed had severe pancreatitis and that in the 43 who survived the acute episode, sequestration was fairly common, in at least 20 per cent.

In addition to the above cases there are reported about 19 cases of acute pancreatitis[30, 43, 47, 55, 58, 71, 75, 114, 120 to 125] in patients known to have diabetes.* In one, the outcome is not stated.[114] One patient survived.[43] The remaining 17 died, most of them in obvious diabetic coma. Not only was the disease almost always fatal, but in many instances it was extremely difficult to make the diagnosis of acute pancreatitis.

In addition to the cases reviewed above, Grott[126] is said to have had a patient who developed acute diabetes during the course of acute pancreatitis which persisted in a chronic form. I have been unable to examine his report. One of Umber's cases has been cited. He has seen diabetes develop in

* In two instances[55, 71] it is not stated that the diabetes existed before the acute illness, though presumably it did.

16 other patients, among 38 with extensive pancreatic necrosis that he has observed.[127] In these he suspected a preexisting diabetic tendency.

Not included in the tabulated cases are a number in which the etiologic relationship of acute pancreatitis to diabetes depends upon the assumption that an initial abdominal crisis was due to the same process as a similar terminal one in which the diagnosis was definitely established, or upon the assumption that the diagnosis made at autopsy explained the initial part of a long continued illness. Frison[128] presented a patient whose diabetes began two months after the onset of abdominal complaints with jaundice. The patient died about eight months later, and showed at autopsy a large pancreatic abscess with common duct obstruction. Frerichs[129] reported two cases. One was a female, age 27, who developed rather severe diabetes at the onset of an attack of abdominal pain, and who presented at autopsy, six months later, a large hemorrhagic cyst of the pancreas. The other was a patient who developed diabetes about one month after the beginning of an acute illness, which was diagnosed at postmortem examination, six months later, as pancreatic abscess. Ponfick[130] had a patient whose diabetes began with an acute illness quite similar to a fatal one terminating in diabetic coma. Autopsy showed hemorrhagic pancreatitis. Norero's[131] patient, likewise, developed diabetes five months after an acute illness quite similar to a subsequent fatal attack one year later which was diagnosed as acute pancreatitis and pancreatic cirrhosis. The cirrhosis was a consequence of the initial attack. There is fair reason to assume that a number of these cases may represent instances of diabetes due to acute pancreatitis.

I have also not included several cases which might be termed temporary diabetes. In 1902, Nash[132] reported the case of a patient who was found to have acute pancreatitis and cholelithiasis on exploration and who had glycosuria when first seen and continued to excrete sugar for six months. Seven months after operation his urine was free of sugar. Hunt[85] and Whipple[101] had patients with acute pancreatitis who required insulin therapy for hyperglycemia and glycosuria, and who recovered completely after a rather long time and remained well. Brocq and Varangot[81] reported the case of a patient who had abundant glycosuria postoperatively which recurred with acetonuria when insulin was first discontinued; the patient was well at the end of three months. Walzel[22] had two patients in whom diabetes developed during acute pancreatitis; they refused operation and subsequently had relief from the diabetes following operative drainage of pseudocysts which had formed. Sodeman[133] reported a similar instance of apparent disappearance of diabetes after operative treatment of a pancreatic cyst.

Warfield,[16] Wilder,[134] Stern,[135] Svartz,[136] Henningsen,[137] Mosenthal[138] and Sobel[139] have presented cases of diabetes which they are inclined to attribute to an acute pancreatitis not proved by celiotomy or autopsy. I have not considered these cases in detail since there is more or less question as to the validity of the diagnosis. A number of these authors feel that even mild, unrecognized cases of acute pancreatitis may either initiate diabetes

TABLE

CASES OF DIABETES BEGINNING ONE YEAR

Author	Diagnosis	Sex	Age	Operation	Autopsy	Onset of Diabetes
Brentano[111] (1899) } Körte[5, 117] (1898)	Acute pancreatitis with abscess	F.	48	Yes	Yes	1½ yrs.
Rollmann[113] (1914)	Acute hemorrhagic pancreatitis with abscess	F.	36	Yes	No	5 yrs.
Vogel[114] (1924)	Acute pancreatitis	F.	26	Yes	No	7 yrs.
Vogel[114] (1924)	Acute pancreatitis	F.	..	Yes	No	6 yrs.
Dunn *et al.*[119] (1926)	Acute pancreatitis	M.	39	Yes	No	6 yrs.
Dunn *et al.*[119] (1926)	Acute pancreatitis	M.	56	Yes	No	4 yrs.
Von Redwitz[14] (1927)	Acute pancreatic necrosis	F.	..	Yes	No	..
Brütt[13] (1927)	Acute pancreatic necrosis	..	..	Yes	No	..
Ney[21] (1929)	Acute hemorrhagic pancreatitis	F.	38	Yes	No	3¼ yrs.
Ney[21] (1929)	Hemorrhagic cyst following pancreatitis	F.	47	Yes	Yes	18 yrs.
Ney[21] (1929)	Acute pancreatitis	F.	46	Yes	No	13 yrs.
Ney[21] (1929)	Acute pancreatitis	M.	35	Yes	No	22 yrs.
Jorns[26] (1929)	Acute pancreatic necrosis	M.	48	Yes	No	2½ yrs.
Bernhard[28] (1931)	Acute hemorrhagic pancreatitis	..	31	Yes	..	11 yrs.
Bernhard[28] (1931)	Acute pancreatic necrosis	..	52	Yes	..	? 8 yrs.
Bernhard[28] (1931)	Acute pancreatic necrosis	..	28	Yes	No	13 yrs.
Bernhard[28] (1931)	Acute pancreatic necrosis	..	29	Yes	No	1 yr.
Joslin[75] (1934) } Gurist[78] (1909)	Acute gangrenous pancreatitis	M.	39	Yes	No	1½ yrs.
Martens[45] (1931)	Acute necrosis	..	..	Yes	No	..
Unger and Sostmann[42] (1931)	Acute pancreatitis	..	..	Yes	No	..
Lemieux[54] (1932)	Acute hemorrhagic pancreatitis	F.	22	Yes	No	1½ yrs.
Downie[58] (1932)	Acute pancreatitis	M.	38	Yes	No	2 yrs.
McWhorter[48] (1932)	Acute pancreatitis	..	..	Yes	No	3 yrs.
deTakats and MacKenzie[49] (1932)	Acute necrosis	..	..	Yes	No	..
deTakats and MacKenzie[49] (1932)	Acute necrosis	..	..	Yes	No	..
Schmieden and Sebening[11]	Acute necrosis	8 cases*		Yes	No	..

or bring about an exacerbation of a preexisting diabetes. Wilder,[134] Hirschfeld,[140] Patrick,[141] Gundersen[142] and Massa[143] have raised the question whether mumps may initiate diabetes through a concomitant pancreatitis. It is striking that in Patrick's review, as this author himself points out, those patients with definite diabetes following mumps had no abdominal pain to suggest acute pancreatitis.

Of great interest are those few available follow-up studies upon patients cured of acute pancreatitis. These are summarized in Table VI. One is at once impressed with the relatively high incidence of disturbance of carbohydrate metabolism. Of 161 patients followed, 14, or about 9 per cent, had diabetes. In addition, about 35 per cent of those studied had some alteration of glucose tolerance. Sebening[8] and Brütt[13] feel that a high percentage of patients have an abnormal glucose tolerance and that there is a tendency toward a return to normal as time passes.

V

OR MORE AFTER ACUTE PANCREATITIS

Character of Diabetes	Remarks
Severe. Died in coma 8 yrs. after operation	Large sequestrum
Severe	Urine negative at time of pancreatitis. Followed 5 yrs.
Rather severe	Urine negative at time of operation and 1 yr. later
Moderately severe	Urine negative at time of acute illness
Well managed on insulin 30 u. B.I.D. Moderate	
Well managed on insulin 10 u. B.I.D. Mild	Trace of sugar found 2 yrs. after operation
No details	Says blood sugar remained normal until patient became pregnant
Blood sugar 450 mg. %	No other details
Mild. Blood sugar 224 mg. %	Had hyperglycemia during early part of course with glycosuria
Moderately severe. Died 3 yrs. later in coma (?) with fracture	
Moderate	Had negative urine during acute illness and during a recurrence 9 yrs. later. Had sequestration of pancreas
Mild	Transient glycosuria 1 mo. postoperatively
No details	No glycosuria before
Died 7 yrs. later with severe diabetes	Large sequestrum—pancreatic fistula for a long time
Died 1 yr. later with severe diabetes and a carbuncle	Large sequestrum. Fistula for 3 mos.
Severe	
Severe	Fistula for 3 mos.
Died in coma 4½ yrs. later	Mother had diabetes. No glycosuria during acute illness
Died of diabetes 4½ yrs. after operation	
Mild	
Managed well on 10 u. of insulin	
Required 70 u. of insulin daily	No glycosuria before
No details	No glycosuria during acute illness
No details	Sugar-free before acute illness
No details	Sugar-free before acute illness
No details	* These 8 cases, included in this series, are not listed separately

As regards changes in carbohydrate metabolism and the very occasional occurrence of diabetes in other diseases of the pancreas, there are a number of reports available in the literature. Very closely related to the subject that has just been reviewed, and probably originating from the same initial lesion, are the cases of pancreatic pseudocysts and diabetes. Beadle[144] and Simsch[145] have presented cases and cited a few others from the literature. Bernhard[146] has also discussed the relationship between pancreatic cysts and diabetes. Wells[147] reported a case of diabetes following posttraumatic calcification of the pancreas and cited another case reported by Grund. Labbé[148] has presented a few cases of pancreatic lithiasis and diabetes and mentioned a few others from the literature. Diabetes apparently following carcinoma of the pancreas is quite rare.[149,151] Sweeney[152] reported a case of subacute pancreatitis in a man with a strongly diabetic family history who developed a temporary diabetes with his illness. Others,[77, 153, 154] have dis-

cussed carbohydrate metabolism changes in chronic pancreatitis. The possible rôle of pancreatic involvement in some cases of biliary tract disease and diabetes has been discussed by several authors.[155, 156]

TABLE VI

FOLLOW-UP STUDIES AFTER ACUTE PANCREATITIS

Author	No. of Cases Studied	Time Between Acute Illness and Follow-Up Study in Years	No. With Abnormal Glucose Tolerance, But Not True Diabetes	No. With Diabetes	Comments
Sebening[8] (1927)	21	½–17	All studied 6 months after operation *	0	* Usually normal when studied a year or more after operation
Brütt[13] (1927)	20	..	Most cases studied shortly after acute illness	1	None had high blood sugar except the instance of true diabetes
Ney[21] (1929)	13	½–23	3*	5	* 2 spilled sugar in urine during test
Tammann[24] (1929)	12	..	6*	0	5 had slightly elevated fasting blood sugar (128–153 mg.) * 2 spilled sugar in urine during test
Jorns[25] (1929)	7	½–13½	5	1	
Stocker[28] (1930)	5	Less than 3	*	0	* All had elevated fasting blood sugar. No further details
Bernhard[38] (1931)	50	..	5*	5	* 25 cases studied. 4 had glycosuria during test
Unger and Sostmann[42] (1931)	16	..	5	1*	*Another case of diabetes had existed at time of operation
Downie[52] (1932)	11	..	2	1	
deKlimko[73] (1936)	6	½–5	3*	0	* Slight changes

Although I have not reviewed the entire literature concerning the diseases mentioned above, it seems apparent that they are associated much less commonly with diabetes than is acute pancreatitis. When one considers the relative severity of pathologic damage in the various conditions, this observation is as might be expected. Furthermore, since these disease processes have a more insidious onset than acute pancreatitis, it is not possible to ascribe to them the causative rôle in the production of diabetes with the relative certainty that can be felt when diabetes ensues after such an abrupt and striking crisis as acute pancreatitis.

The fact has been mentioned that certain authors have felt that mild cases of pancreatitis may result in diabetes. On the other hand, most of those who have had an opportunity to study altered carbohydrate metabolism and diabetes during and following proved cases of acute pancreatitis are impressed with the severity of the pancreatic necrosis in these cases. In general, it seems apparent that these disturbances are due to damage of the islet tissue, though not necessarily of such a nature as to leave anatomic landmarks of the injury. There are no data available to suggest that the destruction of the pancreas is predominantly in one part of the organ or another in those instances in which diabetes has followed pancreatitis, but rather that in most of them there has been almost complete necrosis of the organ. There has

been no consistent diminution in the number of islets of Langerhans or in their histologic appearance, although these observations have been made. Interestingly enough, Körte,[5] who reported one of the early cases, doubted, once he saw the pathologic material at autopsy, that the diabetes had been due to the pancreatic disease. In this case the head was somewhat enlarged, and the body and tail showed to a large extent replacement by fibrosis. Sebening[8] emphasizes the importance of loss of pancreatic tissue during the acute illness in the production of diabetes. Bernhard[38] also feels that the severity of the necrosis, the extent of sequestration, and the persistence of pancreatic fistulae are important factors. Jorns[25] stresses the possible rôle of ensuing chronic pancreatitis. Tammann[24] feels that age is an important factor and that patients with acute pancreatitis who are over 40 run a greater risk of developing diabetes. Bernhard[38] presents data suggesting that this is not true, and certainly it does not seem apparent from the present survey. The importance of familial predisposition to diabetes, mentioned by Umber[127] and Sweeney,[152] does not seem of great significance in the cases reviewed.

Discussion.—In considering acute pancreatitis and diabetes, one may legitimately ask: "What proof have we of a causal relationship?" Diabetes may make its appearance in any decade of life. It is commonly first diagnosed during some acute illness, whether this is an upper respiratory infection, a carbuncle, or some other disease.

It appears obvious, however, that all the evidence speaks in favor of the pancreatic damage as the etiologic agent. In the first place, disturbances of carbohydrate metabolism occur with great frequency during the course of acute pancreatitis. Glycosuria is probably present in 10 to 12 per cent of all cases at one time or another during the acute illness. Hyperglycemia is apparently present with considerable regularity, and altered glucose tolerance, it seems, may be demonstrated in an even higher percentage of cases. Those instances of definite diabetes coming on abruptly during or shortly after the acute illness, such as my case and those collected in Table III, are very impressive. Perhaps little significance could be attached to the cases of diabetes ensuing one year or more after acute pancreatic necrosis, were it not for the fact that, in careful follow-up studies, not only is diabetes found in a significant percentage of cases, but lesser grades of impaired glucose tolerance are observed in a much larger proportion. Altogether the pathogenesis of this type of diabetes seems well established.

As to the factors involved in the production of diabetes, the most striking is that, practically without exception, the cases of diabetes following proved acute pancreatitis have developed after a very severe pancreatitis, generally with widespread necrosis of the organ. Extensive pancreatic sequestration seems to increase the likelihood of diabetes. The fact that, anatomically, acute pancreatitis affects predominantly the acinous tissue rather than the islets of Langerhans is of little concern. Instances are numerous of the so-called idiopathic diabetes in which no anatomic change can be demonstrated in the islet tissue.

Undoubtedly, there are many attacks of mild pancreatitis that escape recognition. It is unlikely, in view of the severity of the necrosis in the proved cases, that these mild cases are responsible for the development of diabetes, though it is possible that such mild attacks may cause exacerbations of preexisting diabetes.

A regards the importance of these findings in the surgical management of acute pancreatitis, the indications are clear. Obviously, every patient should have a complete urine examination before operation. The occasional occurrence of glycosuria may be suggestive, though this finding occurs too infrequently to be of great diagnostic aid. As long as one adheres to the belief that surgical drainage is the treatment of choice, as I do, there may not always be time for extensive blood studies. Each suspected case of acute pancreatitis, however, should have blood drawn for an immediate or subsequent blood sugar examination; and in those instances in which operation must be delayed a few hours because of shock or other circumstance, it will not be amiss to make a glucose tolerance test. Certainly, these studies should be made in instances of suspected mild acute pancreatitis. It will only be through thus accumulating a large amount of data that the present conception of the very high incidence of hyperglycemia and decreased glucose tolerance can be substantiated and the diagnostic value of these procedures confirmed. Likewise, further study will settle the question as to the prognostic importance of these observations. Postoperatively, the urine and blood sugar should be tested frequently and a glucose tolerance test should be made from time to time. Appropriate dietary or insulin therapy should be instituted where indicated. Rich[125] has raised the question as to the possible enhancement of the pancreatic damage through the use of intravenous glucose, because of its action in stimulating secretion of the pancreatic enzymes. Lewis[157] and Wangensteen[158] have, consequently, suggested that glucose should be given sparingly. It may prove of help to avoid a high carbohydrate diet and intravenous administration of glucose unless they are covered by insulin. Those patients who survive their acute illness must be warned to return for frequent follow-up studies. Perhaps early recognition and proper dietary regimen may avert a serious diabetes in those patients showing a mild disturbance of carbohydrate regulation.

SUMMARY AND CONCLUSIONS

(1) A case of severe diabetes mellitus developing in the course of acute hemorrhagic pancreatitis is presented. Other instances of altered carbohydrate metabolism in acute pancreatitis are reported.

(2) The literature concerning changes in carbohydrate metabolism in acute pancreatitis and diabetes as a complication or sequela is discussed.

(3) It is pointed out that glycosuria occurs in about 11 per cent of patients with acute pancreatitis, and that hyperglycemia and decreased glucose tolerance occur in a much greater proportion of cases. The diagnostic importance of the latter tests is discussed.

(4) Diabetes may develop during acute pancreatitis. It may terminate rapidly in coma, or the patient may survive with a persistent diabetes of greater or less severity. It may ensue after a few months or many years. At least 2 per cent of all patients with severe acute pancreatitis develop diabetes, and, of those surviving the acute illness, from 3 to 10 per cent develop this malady. A much larger percentage of surviving patients will have milder grades of altered carbohydrate metabolism. It seems unlikely that mild cases of acute pancreatitis result in diabetes.

(5) It is suggested that these features of the disease be kept in mind in the management of acute pancreatitis, and that systematic follow-up studies be made.

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INDICATIONS FOR LOBECTOMY AND PNEUMONECTOMY IN PULMONARY TUBERCULOSIS*

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PULMONARY RESECTION as a treatment for tuberculosis may be classified in two separate periods: In 1881, Block[1] performed unsuccessfully what probably was the first planned pulmonary resection for tuberculosis. From 1881 to 1895, cases were reported by Ruggi,[2] Tuffier,[3] and others. Tuffier believed that pulmonary resection should be employed when the tuberculosis was localized. He felt that by removal of the primary focus, a spread of the disease might be prevented.

No cases were reported from 1895 to 1934. Probably the poor results previously obtained discouraged surgeons. In addition, the acceptance of collapse therapy was becoming more widespread and the efficiency of thoracoplasty was increasing.

The second period began in 1934. In that year Freedlander[4] performed a successful right upper lobe lobectomy for a tuberculous cavity that could not be closed by pneumothorax. In 1938, Jones and Dolley[5] reported their series of two lobectomies and three pneumonectomies performed in tuberculous patients. They were the first to suggest some of the criteria for planned pulmonary resection in tuberculosis. Scattered cases presented by Beye,[6] Eloesser,[7] O'Brien,[8] Brunn,[9] Rienhoff,[10] Lindskog,[11] Crafoord,[12] and others have brought the total number now reported[5] in the literature to 22. In several of these, tuberculosis was an unexpected microscopic diagnosis following the removal of a lobe or a lung for suppuration.

Many thoracic surgeons now feel that lobectomy and pneumonectomy probably have a definite place in the surgery of pulmonary tuberculosis. As is usually the case with procedures not in general use, no attempt can be made to list clear-cut indications. Our reasons for recommending lobectomy and pneumonectomy at the present time undoubtedly will be modified by further experience. In the present report, six cases of planned pulmonary resection in tuberculosis are summarized (three lobectomies and three pneumonectomies).

From this experience and that of others, particularly of Jones and Dolley, some attempt will be made further to crystallize our present attitude about the indications and contraindications for lobectomy and pneumonectomy in patients with phthisis. Operation upon two of the six cases was performed by Dr. John Alexander, and their inclusion in this series is with his permission. Detailed reports of these two cases will be published subsequently by him.

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Case 1.—L. C., white, female, age 32. On August 3, 1936, a total left pneumonectomy was performed at the University of Michigan Hospital by Dr. John Alexander, assisted by the author. This patient had an atelectasis of the left lung and an advanced fibrostenosis of the left stem bronchus. She was seriously ill because of obstruction of secretions. Thoracoplasty seemed inadvisable because of the marked bronchial obstruction. Dilatation of the stricture was impossible. After a prolonged convalescence she eventually became well and to-day is leading practically a normal life.

It is interesting that this is one of the first planned pneumonectomies in tuberculosis of which we have record.

Case 2.—A. O.'s., white, female, single, age 33, was referred by Dr. Robert Peers, of Colfax, Calif. A total right pneumonectomy was performed by Dr. Emile Holman and the writer at the Stanford Hospital, San Francisco, June 5, 1937. Symptoms of right-sided pulmonary tuberculosis developed in October, 1932. Bed rest alone, later supplemented

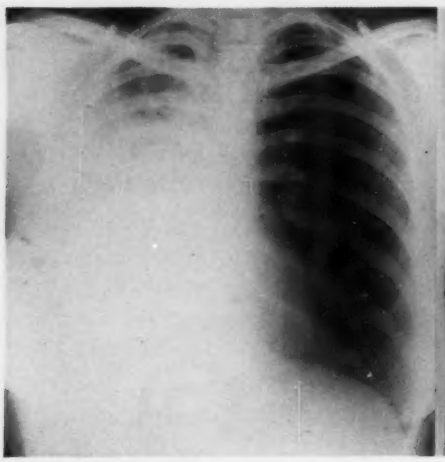

FIG. 1.—Case 2: Postero-anterior roentgenogram prior to thoracoplasty. The base is atelectatic. Questionable areas of cavitation at the level of the fifth and sixth ribs posteriorly.

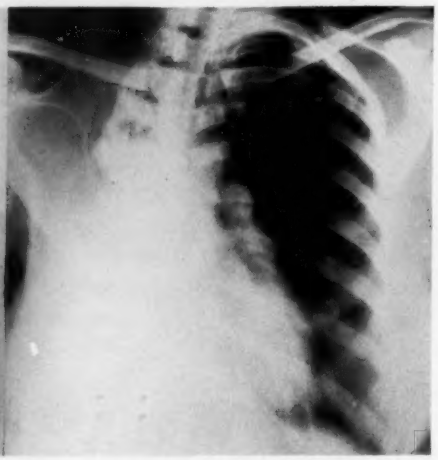

FIG. 2.—Case 2: Roentgenogram with Potter-Bucky technic following ten-rib thoracoplasty. The right lung is completely collapsed. Patient symptomatically unimproved.

by induced pneumothorax for one and one-half years, resulted in slow improvement. During this time she suffered from "asthmatic attacks." The sputum became negative for tubercle bacilli although she still coughed and raised purulent sputum. Her "attacks" were characterized by cessation of sputum for two or three days, fever, and an irritative nonproductive cough. On about the third day, sputum would be produced in large quantities and the temperature would fall. These attacks often occurred at the time of menstruation. A phrenicectomy effected little change in her condition. Roentgenograms showed some suggestion of cavitation in the upper lobe (Fig. 1). Late in 1936, a two-stage, ten-rib thoracoplasty was performed by Doctor Holman. There were no visible uncollapsed cavities following thoracoplasty (Fig. 2). The sputum was decreased in amount but the patient still expectorated from 25 to 50 cc. The harassing cough remained unchanged.

Between the stages of her thoracoplasty, stenosis of the right stem bronchus was demonstrated bronchoscopically. Following the second stage, bronchoscopy again was performed on two occasions (P. C. S.). The right stem bronchus was so narrowed that only a dimple remained. Successful dilatation was not possible.

Indications for Pneumonectomy.—The patient had a persisting chronic infection and

a highly obstructed stem bronchus. Presumably the tuberculosis was arrested since tubercle bacilli were not found in the sputum. The patient's cough was worse following thoracoplasty. It was obvious that the lung was totally atelectatic and that the patient's illness continued because of the lack of drainage of infectious secretions. Pneumonectomy, therefore, was recommended.

Operative Procedure and Subsequent Course.—The right lung was exposed through a posterior incision after regenerated ribs had been removed. The visceral and parietal pleurae were densely adherent. Eventually the hilum was mobilized and a Carr automatic hilar ligature applied. The lung was amputated and the wound closed in layers. Closed intercostal drainage was established. The immediate postoperative convalescence was stormy and bronchopneumonia developed at the left base. Later the wound was opened and packed. Eventually it closed completely by granulation. Clinically, bronchial fistula was never a problem. She has led an essentially normal existence although there has been moderate dyspnea, probably as a result of a slight narrowing of the lower trachea. Recently a few tubercle bacilli were found in her sputum. Bronchoscopic examination revealed a collection of thick pus in the shallow stump of the right stem bronchus. It is possible that a tortuous bronchial tract may persist, leading to a focus in the collapsed interpleural space. The left lung remains clear.

Pathologic Examination.—Dr. James B. McNaught, Stanford Department of Pathology: The lung was shrunken, firm, and entirely atelectatic. Scattered bronchiectases were present. Microscopically, fibrous tissue replaced the alveolar structure. The bronchiectasis was nontuberculous. Most of the tuberculosis appeared quiescent. It was characterized by caseous necrosis with beginning calcification. Only occasional giant cells were seen. Of importance was the fact that the most highly cellular tubercles were located predominantly in the submucosa of the medium and larger bronchi.

Case 3.—A. H., white, female, age 27. Referred by Dr. Elliott T. Smart of Bret Harte Sanatorium. A total left pneumonectomy was performed, October 4, 1938, by the author. Roentgenographically, the original tuberculosis consisted of a minimal lesion in the left lower lobe (Fig. 3). Cough and sputum were out of proportion to the amount of tuberculosis. The sputum was positive for acid-fast bacilli and the patient had a constant wheeze. Accordingly, she was bronchoscoped shortly after admission. Severe tuberculous ulceration and stenosis of the left lower lobe bronchus was found. This was treated with high frequency cauterization five times at monthly intervals. Ulceration almost entirely healed and fibrous stenosis increased. Wheezing disappeared. Following an upper respiratory infection three months later, wheezing again became prominent and bronchoscopy showed extension of the ulcerative lesion to the carina. Following cauterization, partial atelectasis of the left lung developed. There was subsequent clearing, followed by the development of complete atelectasis (Fig. 4). Anterior and posterior mediastinal herniation of the right lung developed. Following further cauterization, the bronchial lesion became a pure fibrous stenosis. Pneumothorax had been attempted without success. There was no change following temporary paralysis of the left phrenic nerve.

Indications for Pneumonectomy.—This patient was observed for six months following the development of total atelectasis. During this time she was always moderately toxic and her sputum persistently contained tubercle bacilli. She had occasional febrile episodes. Bronchial dilatation was attempted, but the patient's symptoms did not abate. Thoracoplasty appeared futile since the lung was already collapsed. The continued toxicity from obstruction of secretions due to the advanced bronchial stenosis made total removal of the lung seem the only surgical procedure offering the patient a chance of a return to health. The patient was in relatively good condition and the opposite lung was clear.

Operative Procedure and Subsequent Course.—The left lung was exposed through a posterior incision with removal of the fifth rib. Adhesions completely obliterated the pleural cavity. The hilar vessels were individually ligated and the bronchus was divided

and closed with silk. The vessels were much smaller than normal. The thoracic cavity was closed without drainage and air was aspirated. The immediate postoperative convalescence was excellent. After the tenth day, the patient became increasingly toxic with fever, cough, and foul expectoration. Repeated aspirations of fluid from the left chest

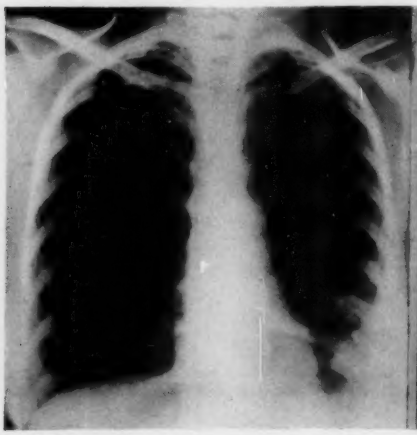

FIG. 3.—Case 3: Postero-anterior roentgenogram. A minimal tuberculous lesion is seen in the left lower lobe.

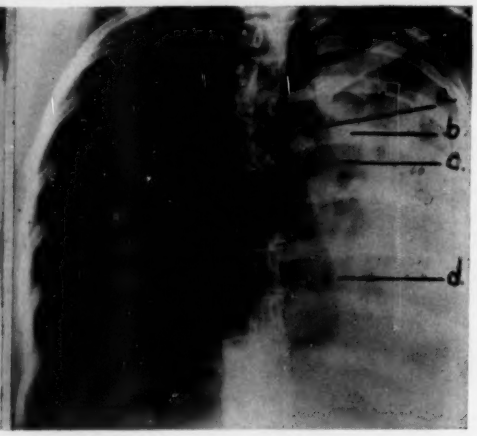

FIG 4.—Case 3: Roentgenogram with Potter-Bucky technic. Total atelectasis of the left lung. Multilocular cavitation at the apex. (a) Carina. (b) Anterior mediastinal herniation of right lung. (c) Stenosis of left bronchus. (d) Posterior mediastinal herniation of right lung.

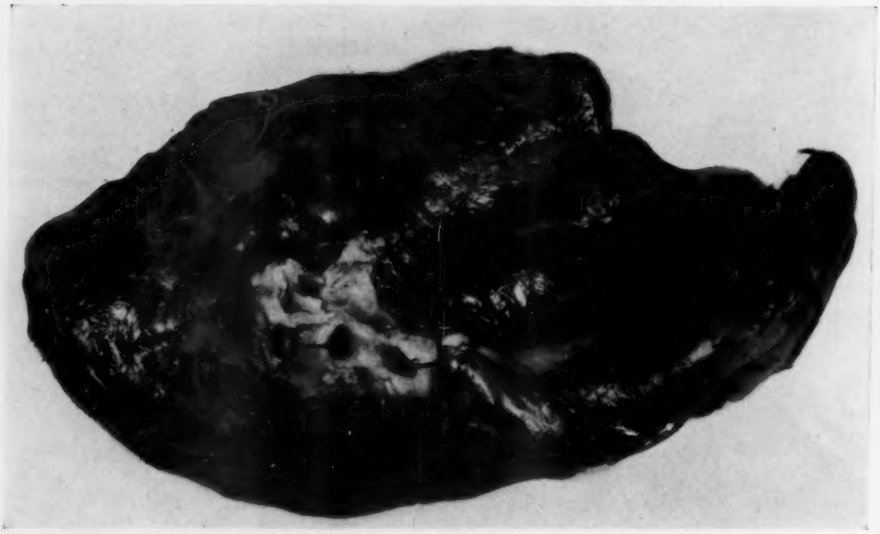

FIG. 5.—Case 3: Mediastinal aspect of atelectatic left lung. The stem bronchus is divided at its junction into upper and lower lobar branches. Considerable mucosal thickening is evident. The lower lobar bronchus is partially obstructed.

showed no evidence of infection at first. Eventually a localized empyema with bronchial fistula became evident. Rib resection was performed but a nontuberculous spill-over infection at the right base already had occurred. The patient was temporarily improved

following drainage by rib resection. Later it was necessary to drain a rectal abscess and the patient died ten weeks following pneumonectomy.

In retrospect it was a mistake not to have drained the pleural cavity at the time pneumonectomy was performed.

Pathologic Examination.—The left lung measured 16x10x3 cm. (Fig. 5). Except for a small portion of the lingula, it was entirely airless. Sections through the main lower lobe bronchus and its branches showed progressively increasing obstruction distally. The mucosa was diffusely ulcerated and the lumina filled with caseous material (Fig. 6). On cut-section, the lower lobe (site of the original lesion) showed fibrous, patchy infiltration and one small cavity filled with caseous débris. In the upper lobe were soft, conglomerate

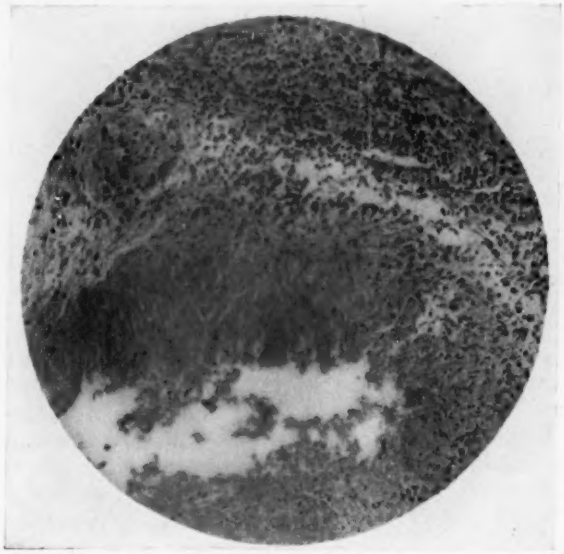

FIG. 6.—Case 3: Photomicrograph showing the obstructed lumen of left lower lobar bronchus. Complete destruction of mucosa by tuberculous ulceration. (×200)

tubercles and several small cavities. The cut-surface was diffusely infiltrated with whitish-yellow, soft caseous material, obviously more active and of more recent origin than the lesions in the lower lobe.

COMMENT ON PNEUMONECTOMY.—There is a striking similarity in the history of these three patients and in the symptoms they exhibited. The syndrome is one which we now invariably associate with progressive ulcerative bronchial disease and subtotal bronchial obstruction. In Case 3 an excellent opportunity was given to observe the progression from ulcerative tuberculous bronchial disease to subtotal fibrous obstruction. In this case, unfortunately, local treatment for the ulcerative disease was not effective in preventing the stenosis. In general, our experience leads us to believe that the chances of curing an ulcerative lesion are better with local treatment than if it is not employed. The clinical appreciation of tuberculous bronchial stenosis with its resultant pulmonary atelectasis is a relatively recent development in tuberculosis work. This knowledge in great part has followed the increasing use of the bronchoscope in patients with phthisis. Eloesser's[13] contributions in

1931 and 1934 were of great value. The prolonged illness of patients with this type of pulmonary disease is now better understood. We are able to evaluate the varied symptoms associated with intermittent obstruction of secretions and the pathologic basis for them. In a broad sense, this type of case, which is not uncommon, refutes the belief of those who feel that pulmonary atelectasis is a favorable prognostic sign in tuberculosis. We feel, on the contrary, that most of these patients cannot become entirely and permanently well without surgery.

No one who has had the opportunity of removing one of these lungs or who has seen them at autopsy can help but be impressed with the difficulties which may follow thoracoplasty. The lungs already are collapsed to the maximum degree. In fact, as illustrated in Case 2, thoracoplasty may be followed by an aggravation of the patient's symptoms, particularly the distressing cough. The pulmonary tissue is extensively carnified. Areas of diffuse pneumonitis are interspersed with small abscess cavities or patches of bronchiectasis. Often this process is predominately tuberculous in nature. As far as the patient is concerned, however, it makes little difference whether or not the tuberculosis is arrested, since nontuberculous suppuration causes continued toxicity if there is bronchial obstruction.

Case 4.—T. L., Mexican, female, age 31. Referred by Dr. Elliott Smart of Bret Harte Sanatorium. A left lower lobe lobectomy was performed, February 25, 1939, by the author. In 1934, this patient was admitted to the San Joaquin General Hospital with a diagnosis of tuberculous pneumonia of the left lower lobe. The sputum contained many acid-fast bacilli. Pneumothorax was instituted immediately but was discontinued after three months because ineffective. A permanent phrenic paralysis was produced. The sputum continued to be positive for acid-fast bacilli. A large cavity was consistently present in the gutter behind the heart but could be seen clearly only by means of oblique or lateral roentgenograms (Fig. 7). No tuberculosis was seen in the upper lobe. An excellent pneumoperitoneum was maintained for one year with no appreciable change in the size of the cavity (Fig. 8). The patient had been treated by various conservative means for a period of five years.

Bronchoscopy revealed a slight narrowing of the left lower lobar bronchus. Purulent secretions came from the left lower lobe. Otherwise the examination was negative.

Indications for Lobectomy.—This patient's disease was sharply limited to the left lower lobe. The upper lobe was entirely free as far as physical examination and roentgenography could determine. The cavity was 4.5 cm. in diameter, old, and thick-walled. It was deep in the gutter and lay immediately in front of the posterior seventh and eighth ribs. In our experience, thoracoplasty for this type of lesion has not been effective. Local rib resection alone has been extremely unsatisfactory and the end-result in several cases has been a total thoracoplasty with the sacrifice of an entirely normal upper lobe. Lobectomy, therefore, appeared to be the most direct approach to the problem.

Operative Procedure and Subsequent Course.—The pleural cavity was opened through a posterior incision in the fifth intercostal space. The lower lobe was densely adherent and extrapleural separation was necessary in the region of the cavity. The hilum was developed, a Roberts-Nelson tourniquet applied, and the lobe amputated. Air-tight rib resection drainage was employed. The postoperative convalescence was not remarkable. About four weeks after operation the drainage tube was covered by the rise of the diaphragm and open intercostal drainage was established more posteriorly for a small hilar empyema. This later became obliterated. The patient expectorates a few cubic centi-

meters of mucoid sputum, negative for acid-fast bacilli. There is no bronchopleural fistula. A cure is expected.

Pathologic Examination.—The removed lobe was shrunken and congested, but not atelectatic. Scattered tubercles were present. The cavity was 5 cm. in diameter and its wall was thickened and fibrosed. There was no obvious bronchial disease.

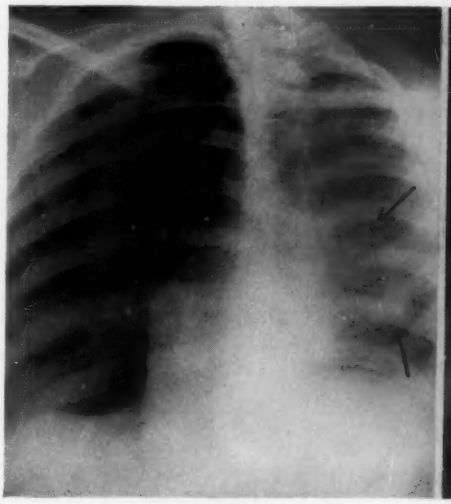

FIG. 7.—Case 4: Left anterior oblique projection. The large cavity is easily seen posteriorly.

FIG. 8.—Case 4: Left lateral projection at the height of the pneumoperitoneum. Transthoracic intracavitary injection of lipiodol. The cavity has not been affected by the pneumoperitoneum.

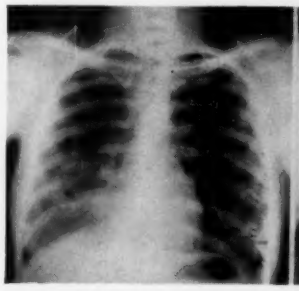

FIG. 9.—Case 5: Postero-anterior roentgenogram showing large tuberculous cavity in right lower lobe. Soft infiltration surrounding the cavity.

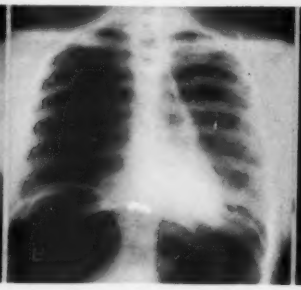

FIG. 10.—Case 5: Apparent closure of large right lower lobe cavity following induction of pneumothorax and pneumoperitoneum.

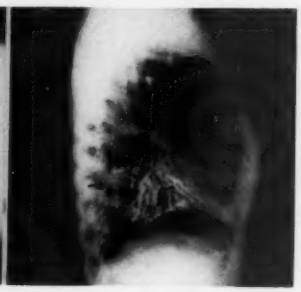

FIG 11.—Case 5: Bronchogram in right lateral projection. There are atelectasis and bronchiectasis of the right lower and middle lobes. The cavity is not filled but lies posterior to the visualized bronchiectases.

Case 5.—M. A., white, female, age 21. Referred from the Medical Chest Service of Dr. Harold Trimble at the Fairmont Hospital. A right middle and lower lobe lobectomy was performed, July 27, 1939, by the author. This patient first was admitted to the Fairmont Hospital with cavernous tuberculosis of the right lower lobe three years prior to lobectomy (Fig. 9). Shortly after admission a pneumothorax was induced. The sputum remained positive and there was roentgenographic evidence of cavity. After ten months, a pneumoperitoneum was induced. Following this procedure the cavity apparently was closed roentgenographically and the sputum promptly became persistently nega-

tive for acid-fast bacilli (Fig. 10). Eighteen months later the patient developed a cold with productive cough and night sweats. Roentgenograms showed that the lower and middle lobes had become atelectatic and that the cavity had reopened (Fig. 11).

On readmission to the hospital, the patient presented a slight elevation of temperature, and was raising large amounts of purulent sputum with considerable difficulty. The sputum was loaded with tubercle bacilli. Bronchoscopy at once revealed the reason for the troublesome cough. Because of atelectasis there was no air exchange in the middle and lower lobes. Purulent, tenacious sputum was "puddled" in the lower lobe bronchus and filled it to beyond the level of the middle lobar orifice. The mucosa was granular and superficially ulcerated. Curettage specimens showed that the bronchitis was not tuber-

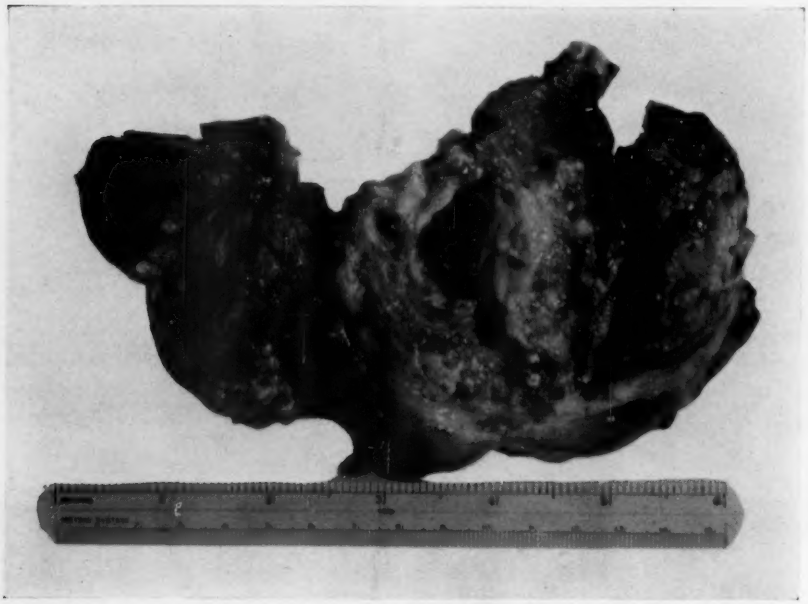

FIG 12.—Case 5: Cut-section through middle and lower lobes. The middle lobe is on the left and shows multiple conglomerate tubercles. The lower lobe is indurated and atelectatic. At its center can be seen a stiff-walled cavity, measuring 4.5 cm. in diameter. At the time of section, the cavity was completely filled with purulent and caseous material.

culous in origin but undoubtedly was due to the irritation of being constantly bathed by purulent secretions. Following repeated bronchoscopies and the institution of postural drainage, cough and sputum diminished and the fever subsided. The mucosa became relatively normal in appearance. The sputum remained persistently positive for tubercle bacilli and there was no change in the roentgenologic appearance of the lung.

Indications for Lobectomy.—After a period of quiescence, this patient developed an exacerbation of her old infection and atelectasis of the right lower and middle lobes occurred. The large cavity reopened. There was no improvement with continuation of conservative measures (pneumothorax and pneumoperitoneum). Because of the position of the diseased lobes and because of the obvious atelectasis and bronchiectasis, it was inconceivable that any type of thoracoplasty would be effective. Lobectomy, therefore, appeared to be the only solution. The pneumothorax was abandoned and the lung was expanded with this operation in mind.

Operative Procedure and Subsequent Course.—The pleura was entered through a posterior incision in the fifth intercostal space. There were firm adhesions surrounding the shrunken, hard, atelectatic middle and lower lobes. There were only a few adhesions

over the upper lobe and there was slight collapse of this lobe during the operation. The middle and lower lobes were amputated following mass ligation of the hilum. The wound was closed in layers and air-tight intercostal drainage employed. The immediate postoperative condition was good. Following transfusion on two occasions, however, she developed severe reactions, became jaundiced, and secreted smoky urine. Death occurred one week postoperatively. A limited postmortem examination showed the right pleural cavity to be dry. The upper lobe was almost completely expanded. There was a slight pleural reaction with early infection. There were scattered old tubercles in the upper lobe and in the left lung. The liver and kidneys were extremely friable, congested, and the site of parenchymatous degeneration. The kidney tubules were clogged with hemolyzed red blood cells. There seemed to be little question but that death was directly due to the transfusion reactions.

Pathologic Examination.—The resected lobes were shrunken and entirely atelectatic (Fig. 12). There were no obvious tubercles in the main bronchi. The middle lobe was soft and flattened and measured 8x4x1.5 cm. The cut-surface was covered with caseous tubercles varying in size from 1 to 5 Mm. The lower lobe was roughly triangular in shape and was greatly indurated. It measured 10x6x5 cm. On cut-section, the center of the lobe was occupied by a large irregular cavity 4.5 cm. in diameter. The walls were thick and the cavity entirely filled with tenacious, purulent and caseous material.

Microscopic examination showed extensive fibrosis, atelectasis, and active caseous tuberculosis. A few submucosal tubercles were present in the main lobar bronchi but these appeared to be of no immediate significance.

Examination of the specimen confirmed our preoperative belief that any type of thoracoplasty would have been entirely ineffectual.

Case 6.—P. B., white, female, age 29. A one-stage right middle lobe lobectomy was performed by Dr. John Alexander, July 7, 1939. The tuberculosis was localized to the middle lobe which was entirely occupied by a solid, fibrocalcareous lesion surrounding a cavity. It was believed that even a total thoracoplasty, including all the anterior ribs and cartilages, might not close the cavity in the cardiohepatic angle. This patient's convalescence was entirely satisfactory.

Comment on Lobectomy.—Indications for lobectomy have differed somewhat from indications for pneumonectomy. In the above cases of lobectomy, stenosis of the lobar bronchus was not a factor. The position of the cavity, however, was important. If the lesions encountered had been in an upper lobe, thoracoplasty undoubtedly would have been performed. The position of these cavities in the lower and middle lobes, together with the associated changes in the pulmonary tissue, made the effectiveness of thoracoplasty doubtful.

Pulmonary resection carries a greater risk than thoracoplasty and cannot be considered as a substitute for it. There are cases, however, in which thoracoplasty obviously is not suitable; others in which it has been performed without cure. Within this restricted group it is apparent that selected cases may be found which can be considered for some type of pulmonary resection. The tuberculosis should be fairly sharply limited to the portion of lung to be resected.

Both lobectomy and pneumonectomy may be considered either as primary or as secondary procedures. In the latter group are those cases of pulmonary resection designed to remove cavity-bearing pulmonary tissue which was not collapsed by a technically adequate thoracoplasty. Cases of this kind are occasionally seen. We doubt the advisability of removing a lobe in which a cavity

has been uncollapsed by a pneumothorax which cannot be completely abandoned, without first obliterating the interpleural space by thoracoplasty.

All cases of planned pulmonary resection which are not preceded by thoracoplasty may be listed as primary procedures. Patients with total atelectasis of one lung and advanced fibrous stenosis of the stem bronchus occasionally suffer from obstructive symptoms, such as intermittent fever and harassing cough, which cannot be relieved by bouginage of the stricture. Pneumonectomy should be considered for such patients, *whether or not* their tuberculosis is apparently arrested. In patients whose bronchial obstruction is due primarily to extensive ulcerative disease, the writer feels that pneumonectomy probably should be deferred until mucosal healing and fibrostenosis have occurred. As with major collapse procedures it would seem futile to perform a pneumonectomy when faced with progressive tracheobronchial ulceration. As an indication for primary lobectomy the location of a large, isolated cavity in a lower or middle lobe is of first importance. The decision is strengthened by the presence of concomitant atelectasis and bronchiectasis, or by the discovery of a stenotic lobar bronchus. Obviously, pneumothorax, phrenic paralysis, and pneumoperitoneum, or a combination of these procedures, will have been tried prior to considering lobectomy.

A further indication is illustrated and discussed by Jones and Dolley, namely, the occurrence of repeated severe hemorrhages from a tuberculous cavity. They feel in these circumstances that lobectomy is safer than thoracoplasty. This view was questioned by Coryllos,[14] and by Janes.[15] The author has had no experience with this possible indication for lobectomy. In certain patients lobectomy certainly should be considered, particularly if the hemorrhage occurs in a tension cavity of the check-valve type.

SUMMARY AND CONCLUSIONS

Six cases of planned pulmonary resection for tuberculosis have been presented. These consist of three lobectomies (one bilobar) and three pneumonectomies. Two patients died following operation, one as the direct result of a transfusion reaction. Two patients are convalescing and there is every expectation of a cure. Two are leading relatively normal lives. Thoracoplasty had been performed unsuccessfully on one patient. In the other five patients, pulmonary resection was preferred as the primary procedure.

We have emphasized that resection is not a substitute for thoracoplasty. Cases occasionally are encountered, however, in which thoracoplasty seems to offer the patient little chance of becoming cured. We believe that under certain circumstances, lobectomy and pneumonectomy may be indicated in the surgery of pulmonary tuberculosis. We have presented our present conception of these indications.

The operative hazards have been discussed.

The author is indebted to Dr. John Alexander, of the University of Michigan Medical School, and to Dr. Emile Holman, of the Stanford University School of Medicine, for

their helpful suggestions and for their permission to include cases in which each was senior surgeon.

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INJECTIONS OF AIR AND OF CARBON DIOXIDE INTO A PULMONARY VEIN*

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It has been repeatedly demonstrated that the injection of air into a systemic vein leads to embolism of the smaller vessels in the lung and that such embolism is not apt to be harmful unless an extremely large volume of air is injected. When air is permitted to enter a pulmonary vein, on the contrary, relatively small amounts may cause death, since the air passes directly through the left heart to the systemic arteries. In this respect, the likelihood of cerebral or medullary embolism has received particular attention. Some chance observations in the laboratory, however, suggested to us that coronary embolism is the chief danger. Consequently, in a series of animals, we have injected air into a pulmonary vein in order to study the manner of death. Furthermore, as a companion study, we have compared the effects of air with those of carbon dioxide, with the possibility in mind that the latter gas might be relatively harmless in view of its solubility and of its property of entering into chemical combination in the blood.

Method.—The experiments were performed upon cats of varying size and age anesthetized by the intraperitoneal injection of sodium amytal. Artificial respiration was maintained through a tracheal cannula. The right and left fifth ribs were removed, the sternum was cut across, and the pericardium opened widely, so that the heart and lungs were clearly in view throughout the experiment. The air or other gas was injected directly into a pulmonary vein by means of an ordinary syringe and needle, a coating of oil preventing any escape of air about the plunger of the syringe. The speed of injection was limited only by the caliber of the needle, the injection requiring from one to six seconds depending upon the volume of air injected. Although most of the injections were made by way of the left superior vein, each of the other pulmonary veins was utilized at times without apparent variation in the result.

Cause of Death.—In each of 30 animals death was finally caused by injecting air into a pulmonary vein. In every instance it appeared that the death resulted from obstruction of the coronary arteries. After the air was injected into the vein, within a second or two one saw air bubbles descending the coronary arterial branches on the surface of the heart.‡ When the dose

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† Recipient of the Dr. J. B. Kass, Research Scholarship in Preventive Medicine.

‡ The uppermost part of the left auricle, *i.e.*, the auricular appendage, often served as an air-trap. After injection of a small dose of air it was sometimes necessary to express the air from this site before it would pass into the left ventricle and make its appearance in the coronary arteries.

was small, only a few tiny vessels near the apex became obstructed; they remained readily visible as branching white lines until solution or absorption of the air. This required from 5 to 20 minutes depending upon the amount of air which had lodged. When only a few such branches were obstructed, there was no visible disturbance of the beat or of the function of the heart.

With larger doses the air filled both coronary arterial trees, even including the main stems.* There it remained. At times a segment of blood interposed in the column of air would be seen to oscillate slightly with the beat of the heart, but there was never any progression of the column to suggest an escape through the capillaries. This complete obstruction of the coronary arteries led to a rapid ischemic failure of the ventricles. They became pale and dilated within two or three minutes. Various degrees of block were followed by ventricular fibrillation and death with the heart in extreme dilatation. This required five or six minutes after the injection. By this time the wink reflex was lost. The animal made violent agonal respiratory movements. A minute or so later the pupils had become extremely dilated and the animal appeared dead although the auricles maintained a regular beat for some minutes longer.

The manner of death, *i.e.*, the behavior of the heart, the appearance of the animal, and the time elements which pertained, were the same as when both coronary arteries are ligated (Moore and Greenberg,[6] 1937; Dennis and Moore,[2] 1938). This fact, together with the absence of convulsions and the occurrence of spontaneous agonal respiratory movements, led to the conclusion that death resulted primarily from coronary obstruction and not from embolism of medullary or cerebral vessels. The terminal cerebral asphyxia evidenced by the loss of reflexes, the dilatation of the pupils, and the agonal respirations was secondary to the failure of the heart.

In 29 of the 30 animals, death followed this cardiac pattern. There was no convulsion. In two of the animals, it was noted that the wink reflex was lost in one eye a minute sooner than in the other; however, in these

* In two animals injections of moderate doses of air repeatedly filled the right coronary artery while causing no embolism of the left artery. In two other animals the tendency was for the anterior descending branch of the left artery to become filled while the circumflex branch of the left artery and the right arterial tree received no air. In young animals with good arterial anastomoses the preservation of two of these three main arterial channels to the myocardium permitted the animal to survive. In spite of irregularities of rhythm and periods of partial dilatation of one ventricle the heart maintained its function. The disappearance of the air from the one vessel it filled required about 20 minutes. In the case of the right artery the air remained visible longest in a circular area about 1 cm. in diameter situated on the anterior surface of the heart just to the right of the interventricular sulcus and about one-third way up from the inferior cardiac border. In the case of the anterior descending artery the air tended to remain longest in a similar area on the right inferior aspect of the cardiac apex just to the left of the anastomotic connection between this vessel and the posterior descending ramus of the right coronary artery. Such areas were visible not only because the airfilled vessels appeared as branching white lines but also because the myocardium was dry, pale and gray in contrast to the moist, red appearance of the adjacent heart muscle.

animals there occurred spontaneous respiratory movements after the heart had ceased all coordinate activity, indicating that until that time the medullary centers were not paralyzed. Consequently, we are skeptical of the dangers of cerebral embolism while the horizontal position is maintained.

That the passage of air to the coronary arteries was independent of the animal's position was shown by Exper. 27, the one instance in which a convulsion did occur. In this experiment a sublethal dose of air was repeated—first with the animal board tilted to 30° head-down, then with the board tilted 30° head-up, and, finally, with the board horizontal. In the three positions, there occurred apparently identical amounts of coronary embolism, the air requiring in each instance about 15 minutes for absorption. Next the animal was given a lethal dose of air with the board horizontal, and, as it was dying with the ventricles fibrillating, convulsions occurred in the hind legs. We suppose these convulsions signified cerebral embolism although they occurred 34 minutes after the injection made with the head elevated. In three of the other experiments, injections were made with the animal board inverted so that the animal was suspended in a quadrupedal walking position. Death occurred from coronary obstruction just as when the animal was lying upon its back.

We do not infer that regardless of position all air injected by way of a pulmonary vein passes into the coronary arteries, but rather that, being the first aortic branches, the coronaries receive a considerable proportion of the air. In every animal we studied the coronary embolism of itself caused death, leading as it did to ventricular fibrillation.

Fatal Dose of Air.—Ordinarily, injections of volumes up to ¼ cc. per pound body weight were tolerated without sufficient disturbance of the heart to harm the animal. This dose would amount to 37.5 cc. of air into a pulmonary vein of a man of 150 lbs.* Doses exceeding ¼ cc. per lb. were apt to be fatal and doses exceeding ½ cc. per lb. were regularly fatal.

Effects of Carbon Dioxide.—In a number of animals we injected pure carbon dioxide into a pulmonary vein.† It appeared to be harmless. We made repeated injections, some as large as 3.0 cc. per lb. body weight, a quantity

* In six cats, we determined the ratio of heart weight to body weight. The figure ranged from 0.31 per cent to 0.55 per cent with an arithmetical average of 0.39 per cent. Smith[8] (1928) found that in man the normal heart averaged 0.43 per cent of body weight in the male and 0.40 per cent in the female.

† Samples were taken from a number of tanks of commercial carbon dioxide purporting to be pure. In every instance chemical analysis proved air to be present and injection of such a sample into a pulmonary vein resulted in coronary embolism in proportion to the amount of air in the mixture. Thereafter, we generated our own carbon dioxide by pouring concentrated hydrochloric acid over marble chips in a small glass flask. After the first violent bubbling had ceased the flask was closed with a one-hole rubber stopper carrying a glass tube. This tube was fitted with a rubber connection of a size to fit the nozzle of a Luer syringe. After a few minutes to permit all air to be displaced from the flask and tubing, the syringe was attached and the carbon dioxide allowed to flow into it by virtue of its own pressure, the plunger of the syringe being sealed with oil. With these precautions it was possible to obtain carbon dioxide practically free of air.

corresponding to 450 cc. for a 150 lb. man. In one animal we injected a dose of 2.0 cc. per lb. body weight three times in four minutes for a total dose of 6.0 cc. per lb. No lasting embolism resulted. Thirty minutes later the same animal suffered the typical coronary embolism death from an injection of one-sixth this volume of air.

During the injection of the carbon dioxide there was a loud "slap-slap-slap" sound—the "mill-wheel" murmur. The gas was seen to fill both coronary trees within a few seconds but in 15 to 20 seconds it was entirely replaced with blood. Even the tremendous doses employed caused too short a period of coronary obstruction to disturb the heart's rhythm. Although immediately after the injection the vessels were filled, within a few seconds a column of blood could be seen advancing down each artery. With every systole of the heart this column of blood advanced several millimeters. In eight or ten beats of the heart only a little of the gas remained visible. This remainder vanished in another few seconds except in instances when the gas was contaminated with air, in which cases a varying number of the smaller arterial branches remained visibly obstructed for some minutes.

Discussion.—In considering the dangers attending the entrance of air into the circulation one must distinguish between the systemic and the pulmonary veins. The fear that the accidental entrance of air into a systemic vein may result in sudden death has been dispelled to a great degree by the repeated demonstration that large volumes of air can be injected into the veins of animals without fatal results. In the dog from 3.5 cc. (Harkins and Harmon,[4] 1934) to 7.0 cc. (Wolffe and Robertson,[11] 1935) per lb. body weight is required to kill when given into the femoral vein in a single injection. Richardson, Coles and Hall[7] (1937) tried a method of continuous injection at a slow rate and in one dog injected 3,910 cc. over 87 hours' time before death occurred. Similar experimental results can be found as far back in the medical literature as one cares to go. In 1889, in a demonstration before the Philadelphia County Medical Society, Dr. H. A. Hare injected 60 cc. of air into the jugular vein of a 12-pound dog without harmful effect. In describing his experiments, Hare[3] wrote: "Magendie states that he has thrown, with all the force and celerity of which he was capable, 40 or 50 pints of air into the veins of a very old horse without his dying immediately, and Cormack (1837) blew the contents of his chest, twice filled, into the jugular vein of a horse before the animal exhibited any signs of uneasiness. Barthelmy has also found that in six horses, weakened greatly by the withdrawal of blood, as much as four to six liters of air must be introduced intravenously to cause death, and estimates, in consequence, that a man weighing 136 lbs. would be killed only by two-thirds of a liter." Hare concluded that "enormous amounts of air must enter a vein to cause death," and that "no such quantity can possibly find its way into a vein which has been injured with the knife of the surgeon."

Numerous studies have shown that air which enters a systemic vein is churned with the blood in the right ventricle to form a froth. Because of its compressibility this froth interferes to some extent with the expulsion of blood

from the ventricle. This phase, which is accompanied by a loud murmur, lasts but a few moments. The froth is ejected into the pulmonary artery and the bubbles of air lodge in the smaller vessels of the lung. Nitrogen is so sparingly soluble that the vessels remain obstructed for many minutes. Although massive doses of air may cause death in this manner, the pulmonary vascular bed is so capacious that large amounts are tolerated without sufficiently widespread obstruction to bring the lesser circulation to a stop. Furthermore, the pulmonary vessels are such an effective barrier that ordinarily none of the bubbles reach the left heart to lodge as emboli in the coronary or cerebral circulations.

In the case of a pulmonary vein, however, there is no capillary barrier to prevent the air reaching the left heart. As a result, small quantities, by lodging in certain medullary or coronary vessels, may cause cessation of respiration or failure of the heart. Van Allen, Hrdina and Clark[9] (1929) found that the dog's maximum tolerance for air injected into a pulmonary vein was only 1.5 cc. per Kg. body weight, whereas one dog survived an injection into the jugular vein of 76 cc. per Kg. In the experiments we have reported, the maximum by way of a pulmonary vein for the cat was 1.1 cc. per Kg. Van Allen, Hrdina and Clark stressed the principle of "air buoyancy." Because of the gravity factor the air tends to pass to the uppermost vessels. These workers found that with the animal in the dorsal, recumbent, horizontal posture the arch of the aorta is high and serves as a trap, as a result of which much of the air passes out the great arch branches to the head, neck, and upper extremities. With the head down little of the air passes to the fore part of the body but the coronary vessels are heavily involved.

In our experiments with cats little evidence of harmful cerebral embolism was encountered. On the contrary, regardless of the position of the animal, a fatal coronary embolism was the rule. Considering the position and configuration of the aortic sinuses it would be our judgment that the ventral recumbent position with the head down might result in the air passing by the coronary orifices without entering them. Except in occasional operations, however, this position would be impracticable. Moreover, in view of our experiments, we feel that there is little hope of lessening the dangers of air embolism by placing the patient in any special position.

To compare oxygen embolism with air embolism, Harkins and Harmon[4] (1934) calculated from the oxygen-unsaturation of venous blood that the minimum fatal dose of oxygen would be approximately 10 per cent greater than the minimum fatal dose of air. In a few animals in which we injected oxygen taken from commercial tanks which were labelled "pure," the gas appeared to produce just as lasting embolism as did air.

In this respect, the contrast between carbon dioxide and either air or oxygen was striking. Pure carbonic acid gas would not produce a lasting embolus. In explaining this difference one should bear in mind that carbon dioxide is an extremely soluble and highly reactive substance. We suppose that its solubility and its capacity as a weak acid to unite with the alkaline blood

buffers are the chief factors accounting for the rapid disappearance of gaseous carbon dioxide from the vessels. We do not believe that the gas escaped through the capillaries into the venules, for we never saw bubbles ascending the coronary veins. Furthermore, if one watched large bubbles of carbon dioxide gas in the middle of a column of blood, he saw them suddenly vanish as though they had dissolved in the blood.

The finding that pure carbon dioxide gas does not produce stable emboli when it is introduced into a vein, suggests several practical applications. It might well be substituted for air to provide the desired degree of collapse during closed intrapleural operations such as, for example, the endoscopic severing of pleural adhesions. While its absorption would probably be too rapid for use in therapeutic pneumothorax, it should be a very safe substance for the exploratory initial fill in a patient in whom pneumothorax is desired. Although the fact that carbon dioxide is much heavier than air suggests that it could be used in open thoracotomy, any admixture of the gas with air would lessen the protection from embolism. The authors have injected large amounts of carbon dioxide into the pleural cavity of the cat and know that the gas has been used without harm for pneumoperitoneum. However, since we have not injected it into the pleural cavity of man, we can make no recommendations in this regard other than to emphasize the necessity for the carbon dioxide to be pure if air effects are to be avoided.

We have been able to find only one previous report of the injection of carbon dioxide into veins. In 1924, Colle[1] reported that it produced embolism just as did air. We suspect that he was led astray through the use of ordinary commercial carbon dioxide, which, as we have noted, is often heavily contaminated with air.

In conclusion, it might be stated that the embolic effect of air requires an explanation. If blood passes through the smaller vessels, why cannot air? Apparently the lodging of air in the vessels centers about the fact that the air is present in bubbles having a resistant liquid film. Wilson and Ries[10] (1923) showed that with certain colloidal solutions the surface films of the foam behave as gel-like plastic solids rather than viscous liquids. As a result the superficial viscosity may be more than 1,000 times that of water. Such bubbles are extremely resistant to rupture. Similarly, Langmuir[5] (1938) has emphasized the viscosity and elasticity of certain protein films on water and believes that in such films the protein molecules actually undergo a form of "denaturation" to form a homogenous, continuous structure. It is our supposition that in air embolism the films of blood about the air bubbles have assumed to some degree this same rubber-like quality.

SUMMARY

A considerable proportion of the air injected into a pulmonary vein of the cat lodged as emboli in the coronary arteries. This occurred regardless of the animal's position. In 30 consecutive experiments, the injection of a volume of air equalling or exceeding 0.5 cc. per lb. body weight caused a typical

coronary death. In only a few cases was there accompanying evidence of cerebral or medullary disturbance.

Upon injecting pure carbon dioxide into a pulmonary vein it was found that this gas would not produce a stable coronary embolus. Although an injection of 2 cc. per lb. body weight filled the coronary vessels, the gas was entirely taken up by the blood in 15 to 20 seconds and the heart was not visibly affected.

The appearance and behavior of the heart following injections of air and of carbon dioxide are described and the mechanism of air embolism is discussed. In relation to the absence of harmful effects from the intravenous injection of carbon dioxide certain practical applications are suggested.

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CONSERVATIVE ELECTROSURGICAL EXCISION OF SUBESOPHAGEAL, CHRONIC PENETRATING OR ACUTELY PERFORATED GASTRIC ULCER

REPORT OF AN UNUSUAL CASE THUS TREATED—WITH GOOD END-RESULTS

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CHRONIC, indurated, penetrating or acutely perforated gastric ulcers, situated in the subesophageal area of the stomach, present, from the standpoint of feasible surgical attack, difficult and hazardous problems. Access to the lesion may be so difficult and impractical as to preclude the possibility of a partial gastrectomy. Total or subtotal gastrectomy in comparatively young patients is repugnant except for a malignant neoplasm. Gastro-enterostomy alone offers little, the beneficial reparative changes anticipated in the ulcer, through drainage and chemical change, possibly being nullified, as suggested by Deansely,[2] by too great a distance from the lesion. Attempt at direct excision, or cautery destruction of the ulcer in addition to the performance of a gastro-enterostomy may, in a subesophageal lesion, be fraught with great hazard.

In 1936, Wells,[1] of Liverpool, reported four cases of chronic subesophageal gastric ulcers which he had treated, with most gratifying results, by performing an antecolic Pólya-Moynihan partial gastrectomy, the line of gastric section being made below the level of the ulcer, so that the ulcer was left in the remaining portion of the stomach.

Deansely,[2] of Wolverhampton, independently devised the same method of dealing with these cases and reported favorably on four. Walker,[3] in reporting on six additional cases operated upon by this method, states: "Of these ten cases [his own and those of Deansely], nine have been traced and eight can be regarded as cured; they are leading normal active lives, having no symptoms except a little feeling of fulness after meals." Pauchet and Luquet[4] strongly advocate the so-called "groove resection" for ulcers in the upper third of the stomach. Where the ulcer is not too large and lies in an accessible position on the lesser curvature, this procedure would seem the preferable method, as it removes the ulcer *in toto*. Where a very large indurated gastric ulcer lies in a direct subesophageal position, as was found in one of our cases, or where an acute perforation presents, as was true in another, this procedure would not be feasible. Jejunostomy with physiologic rest of the gastric function may or may not result in cure. In the event of failure, the economic and time loss is very disappointing to the patient.

Transgastric approach, with actual cautery treatment of the ulcer and suture from within, may temporarily be satisfactory, but is prone to be fol-

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lowed later by recurrence of symptoms and reidentification of the ulcer crater on roentgenologic study. The location and size of the ulcer in the case we are reporting was unique in our experience, and the technical procedure employed was one which, at the time, seemed to offer little promise of being more than temporarily beneficial. The unexpectedly smooth convalescence and subsequent freedom from all previous symptoms merit a report and a description of the technical procedure followed. In our opinion and experience, it

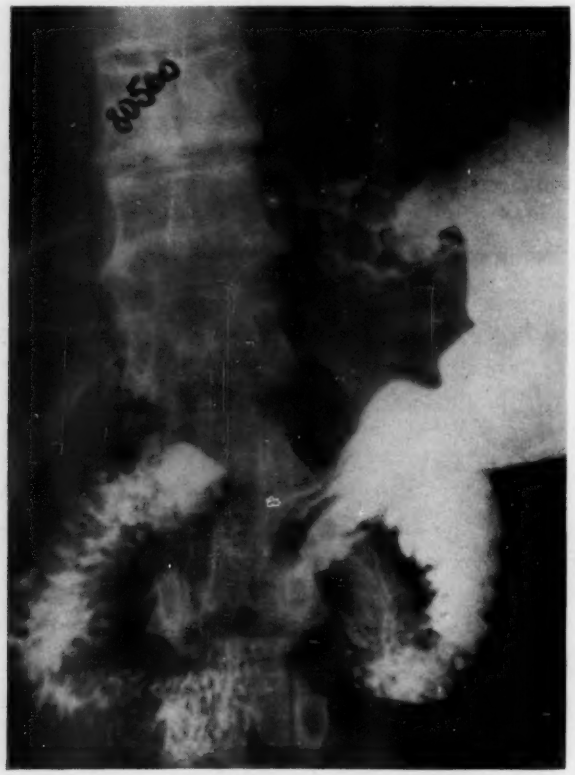

FIG. 1.—Roentgenogram, September 8, 1937, showing large, subesophageal gastric ulcer.

offers "another way out"—a comparatively safe and easy one—for the surgeon confronted with a situation where a "gutter resection" is impracticable and a Wells partial gastrectomy, leaving the ulcer in the gastric remnant, would be a formidable and hazardous procedure.

Case Report.—Clinic No. 80500: T. W., white, male, age 41, married, truck driver; admitted September 7, 1937. Chief Complaint: Stomach trouble.

Previous History.—Appendicectomy elsewhere, in 1923. For past seven years has had periodic "stomach upsets"; burning epigastric distress with belching, especially when stomach was empty; sometimes relieved by food and soda.

Present Illness.—For past three months these symptoms have persisted incessantly. Very often the taking of food seems to "set the stomach on fire." The epigastric pain has steadily increased in severity. There had been no improvement under a rigid ulcer

dietetic and medicinal regimen. The patient had lost 25 pounds during the past four months.

Physical Examination.—Rather frail, sickly looking man with typical stomachic facies. Head, throat, chest and extremities negative. Blood pressure 105/65. Tenderness was elicited on deep pressure high in epigastrium; otherwise negative.

Laboratory Data.—Blood: hemoglobin 80 per cent, red blood count 4,450,000, leukocytes 9,500; Wassermann negative. Gastric analysis: Total acid, in three-quarters of

FIG. 2.—A large, indurated, subesophageal gastric ulcer. All organs except stomach were normal. The stomach was entirely free from abnormal attachments, even over the area where the lesion was situated. A malignant lesion on an ulcer base was suspected.

an hour, 90, in one hour, 84, in one and one-quarter hours, 74; free hydrochloric acid, in three-quarters of an hour, 64, in one hour, 58, and in one and one-quarter hours, 48.

Roentgenologic Examination.—September 8, 1937: "There is a large gastric ulcer in the upper part of the upper third of the lesser curvature of the stomach." November 11, 1937: "The ulcer in the upper area of the lesser curvature previously described is confirmed and is more conspicuous than at the previous observation" (Fig. 1).

Staff Consultation.—May be large gastric ulcer or, judging from size of crater defect, a malignant neoplasm. Exploratory celiotomy advised.

Preoperative Diagnosis.—Gastric ulcer or neoplasm. *Postoperative Diagnosis:* Large penetrating subesophageal gastric ulcer.

Operation.—November 16, 1937: Under spinal pontocaine anesthesia, the abdomen was opened through a long, left paramedian, epigastric incision. *Operative Pathology:* All organs except stomach were normal. The stomach was entirely free from abnormal attachments, even over the area where the lesion was situated. On first palpating the cardiac end, a large neoplasm was suspected. The lumpy induration was decidedly

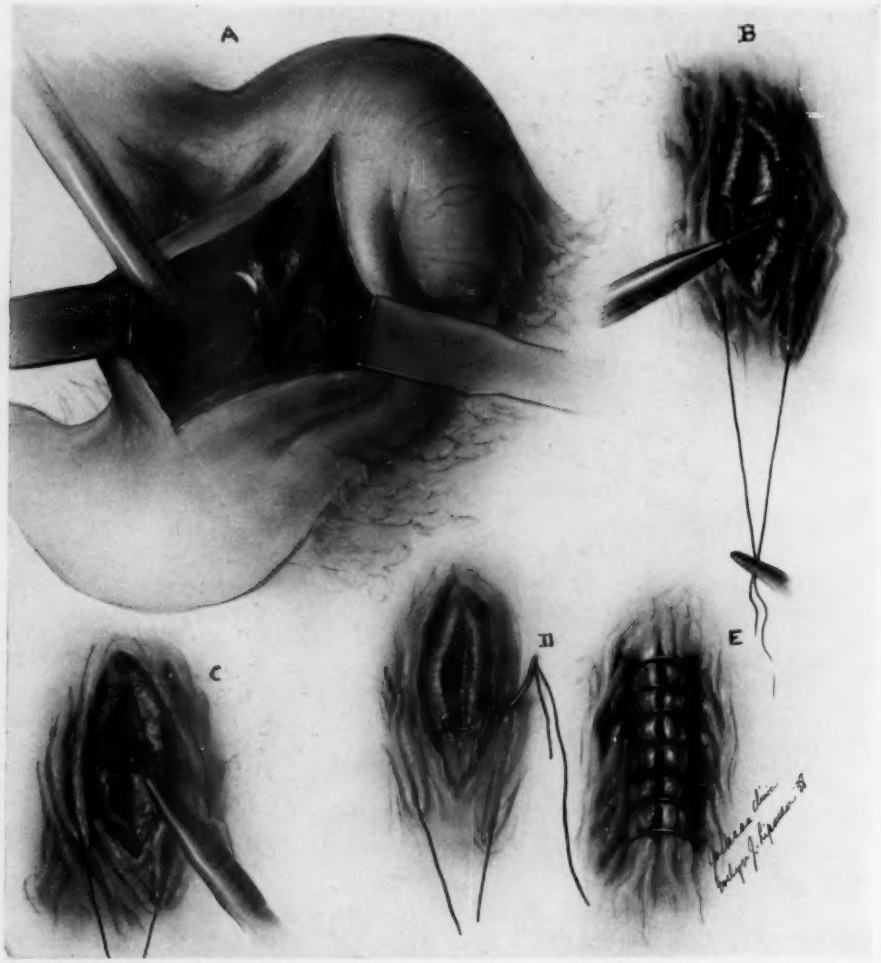

PLATE I.—(A) Transgastric approach. With a gooseneck Cameron light, the lower end of ulcer was inspected. When the stomach was quiescent, the ulcer assumed an oval shape 6 cm. long and 3 cm. wide; when a peristaltic wave occurred it changed to a slit-like form, the contracting edges firmly grasping the palpating finger.

(B) With the radio-loop instrument, thick shavings of crater edges were removed for microscopic examination. No suspicion of carcinoma was found.

(C) The base of the ulcer was sterilized with the ball-pointed instrument (coagulating current).

(D) Heavy, interrupted 30-day chromic gut sutures were placed, needles passing through serosa and muscular layers.

(E) Appearance after all interrupted chromic gut sutures had been placed.

humped-up directly below the esophageal entrance and extended down the lesser curvature for several inches, being decidedly thicker on the posterior gastric wall than on the anterior (Fig. 2). A "gutter resection" was not feasible. The wide extent of the massive induration excited the suspicion that a malignant degeneration had occurred in a chronic

ulcer base. If so, a total gastrectomy would be futile. It was deemed advisable to ascertain the underlying pathology by direct intragastric inspection and biopsy.

Transgastric Approach.—Several heavy silk traction sutures were placed high on the anterior gastric wall and a four-inch oblique incision made (Plate I A).

The stomach, aside from the lesion, was completely flaccid and empty, continuous gastric suction having been maintained for the preceding 12 hours. With ribbon retractors holding the edges of the gastric wall far apart, it was possible, with a gooseneck Cameron light, to inspect the lower end of the crater. When the stomach was quiescent,

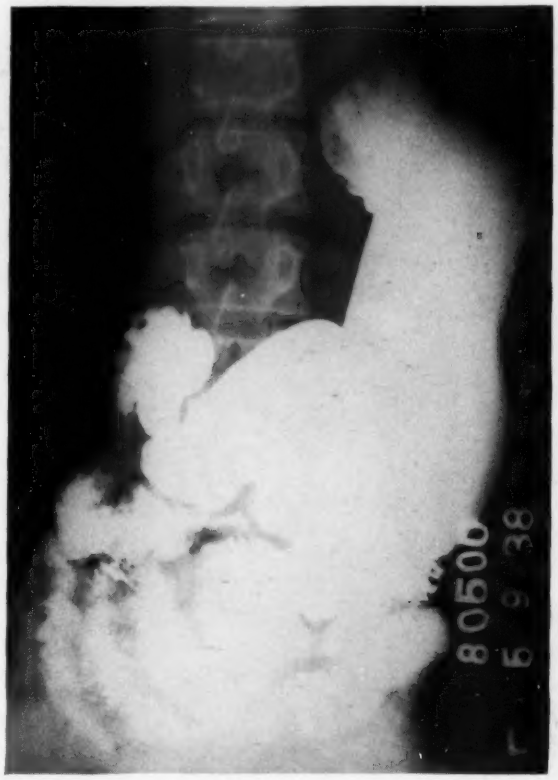

FIG. 3.—Roentgenogram of stomach one year and two months after operation. The site of the former ulcer defect is smooth.

the crater assumed a longitudinal oval shape, 6 cm. long and 3 cm. wide; when a peristaltic wave occurred, this changed to a slit-like form, the edges approximating each other. A finger inserted into the crater was firmly held by the contracting edges. The crater, throughout its entire length, had penetrated through the musculature of the gastric wall. Counter palpation with a finger of the other hand over the crater area revealed a well-formed, thick, plastic base protection.

A heavy silk traction suture was applied to the inside of the posterior gastric wall just proximal to the lower end of the crater. This helped materially in drawing down the crater.

With the wire loop electrode of the electrosurgical instrument several 1 cm. thick shavings were removed from the crater edges and examined (Plate 1 B). They showed only chronic inflammatory changes with no suspicion of carcinoma. Both edges of the crater were repeatedly beveled down with the loop, using alternately the cutting and coagu-

lating currents until definite muscular tissues were exposed from end to end, and practically normal gastric mucosa fringed the edges. This assured removal of the ulcer except for its base. There was no appreciable hemorrhage from the "looping excision," small bleeding points being directly controlled with the coagulating current.

A ball-pointed electrode was then applied thoroughly over the base of the crater (coagulating current) to sterilize it (Plate I C).

The two edges were then approximated by 30-day No. 2 chromic catgut interrupted sutures, inserted 1 cm. from the edges and passing through the entire gastric wall but not penetrating the plastic base (Plate I D). The proximal sutures, after tying, were left long and served most efficiently as tractors in placing the next higher-up suture. Step by step the denuded stomach wall edges were thus approximated. The extreme upper end was quite difficult but was satisfactorily accomplished (Plate I E). Every few moments a gush of esophageal mucus flooded the upper end of the area. An examining finger detected the esophageal opening at 3 cm. above the highest suture.

After closing the gastric exploratory incision, a posterior gastro-enterostomy was performed.

Convalescence was uneventful. Continuous gastric suction was maintained for ten days. The patient was entirely free from his former symptoms immediately following the operation and has remained so up to the present time, January, 1939. The wound healed by primary intention.

Roèntgenologic Report.—January 12, 1938: No defect is seen in the stomach other than a gastro-enterostomy. The site of the former ulcer defect is smooth (Fig. 3).

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TUBERCULOSIS OF THE STOMACH

A CLINICAL AND PATHOLOGIC STUDY

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TUBERCULOSIS of the stomach, whether encountered as an isolated lesion, or as part of an active tuberculous process, is a very rare condition clinically or in necropsy material. It is remarkable to note the relative infrequency of gastric tuberculosis in view of the high incidence of pulmonary tuberculosis, especially when the cases show a deficient acidity and gastric secretion. One would think that the tubercle bacilli should find an ideal medium in the stomach since the latter is devoid of the usual bacteriologic protection supplied by the normal secretion of the gastric mucosa and thus rendering the organ more susceptible to the tuberculous infection. Since tuberculosis of the stomach is one of the rarest manifestations of tuberculosis in the body, it is possible that the stomach has some peculiar natural immunity to the tubercle bacilli, a protection lacking altogether in the intestinal tract.

Because of the rarity of tuberculosis isolated to the stomach, it is doubtful whether it has ever been diagnosed clinically before operation. Even during the operation, the diagnosis is usually not suspected.

As to the incidence of the disease: Broders,[1] in 1917, found 49 authentic cases and 118 probable cases of stomach tuberculosis reported in the literature. In 1931, Good[2] reported three cases of stomach tuberculosis in a series of 7,416 consecutive gastric operations performed at The Mayo Clinic. Since his report, three additional cases have been reported by the Clinic. The same author, in a total of 71,871 necropsies, found that 141 cases, or about 0.2 per cent, had tuberculosis of the stomach, while necropsies of 15,165 tuberculous subjects yielded 80 cases, or 0.52 per cent.

From 1929 to 1938 (inclusive), there were 11,480 consecutive autopsies performed at the Cook County Hospital. During this period, there were 288 cases of pulmonary tuberculosis and in 242 additional cases pulmonary tuberculosis was found as an incidental finding, the patients dying of some other unrelated cause. In the former group of cases, there was *one* instance of tuberculosis of the stomach encountered, an incidence of 0.35 per cent. There was also a third group of 24 cases in which a generalized tuberculous adenopathy was the primary cause of death. In this group, one case of tuberculosis of the stomach was present. Thus, in 554 cases of tuberculosis coming to autopsy, the stomach was involved in *two* cases, while during the same

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period of time, only *one* case was encountered in 75,000 surgical specimens.

One may distinguish, pathologically, two types of tuberculosis of the stomach: (a) Miliary tuberculosis, whereby the stomach contains single caseous tubercles located in the submucosa, or on the serosa, and is a part of the stage of generalization; and (b) ulcerative tuberculosis which is characterized by numerous shallow, irregularly shaped ulcers with overhanging margins and grayish-yellow bases, that rarely penetrate the muscular layer, and which may eventually cause scarring and shrinking of the stomach, simulating syphilis or carcinoma. The ulcer type is the predominating lesion, being present in 80 per cent of the cases of gastric tuberculosis reported.

The sources of infection are thought to be (a) by direct invasion of the mucosa; (b) by bloodstream; (c) by the lymphatics; or (d) by direct extension.

Two of our cases were of the ulcerative type, and only in one was the tuberculous process isolated to the stomach, producing clinical manifestations. Tuberculosis of the stomach is usually an incidental finding and may or may not produce clinical symptoms. In our series of four cases, only one was associated with clinical manifestations and it is this case that we are reporting in detail.

Case Report.—L. B., male, colored, age 34, was admitted to a medical ward, March 4, 1936, with the entrance diagnosis of carcinoma of the stomach. He stated that he had been in very good health up to six months ago when he began to notice epigastric distress that came on during, or shortly after, eating. This pain was dull and aching in character and radiated to the back, usually lasting about one and one-half hours, and was not relieved by alkalies, food intake or bowel movement. All types of food brought on the attack. He was freed completely of pain and distress only if he took no food. If pain was present it would be aggravated by walking or moving around and was not associated with nausea or vomiting. The pain had lately become more intense, lasting longer after each meal, so that patient had recently resorted to starvation. He had lost 20 pounds in six months, from 140 pounds to 120 pounds.

His past history was essentially negative. He had had no surgical operations. Other than the usual childhood diseases his past health had been good. He had had gonorrhea twice, the last attack occurring five months before, which had lasted two months. A chancre was noted two and one-half years before and it was treated with numerous "shots" in the hips and arms. Although he suffered from constipation and had to resort to laxatives he had never noticed blood or mucus in his stools. He had been married twice. He had divorced his first wife, who was living and well, and who had been pregnant twice; the first pregnancy was terminated by an induced abortion. The second lived to the age of four and one-half years. Death of this child was due to miliary tuberculosis. His second wife, living and well, had had no pregnancies. His family history was essentially negative.

Physical Examination.—Temperature, 97.4° F., pulse rate 60, respirations 18. Blood pressure 96/58. He was well developed but undernourished. The pupils were equal and reacted sluggishly to light. The clavicular fossae were prominent. The examination of the lungs and heart was apparently negative. The abdomen was scaphoid in the region of the epigastrium. A small, firm mass the size of a tangerine was palpated just to the right of the midline in the epigastric region. The liver, kidneys and spleen were not palpable.

Laboratory Data.—W.B.C., 6,850; R.B.C., 4,340,000; Hg., 80 per cent. Urine exam-

ination was negative. Roentgenologic examination of the stomach and duodenum showed an "annular filling defect in the pars pylorica with absence of rugae throughout the entire stomach, very suggestive of carcinoma" (Fig. 1). An Ewald test meal revealed a total acidity of nine units (Töpfer's method), no free hydrochloric acid, and a total gastric content of 140 cc. No blood was noted in the stomach contents or feces. A blood Wassermann test was negative.

The case was transferred to surgery as a case of carcinoma of the stomach, with syphilis to be considered.

Operation.—March 11, 1936: Through an upper midline incision, the stomach and duodenum were exposed and a mass was found involving the pylorus and distal one-third of the stomach. The mass was moderately hard in consistency. The pyloric ring was

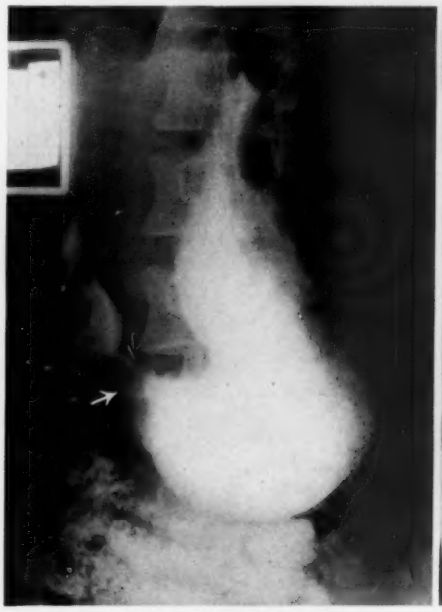

FIG. 1.—Roentgenogram showing involvement of the pyloric end of the stomach, with evidence of obstruction.

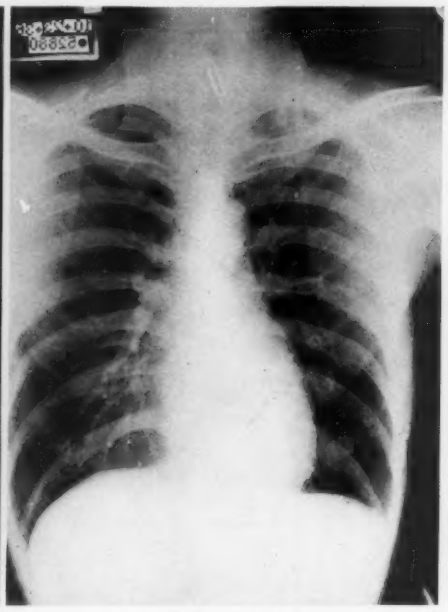

FIG. 2.—Roentgenogram of the chest, taken seven and one-half months after partial resection of stomach, showing several calcified shadows in the left apex.

markedly stenosed. The lymph nodes along the lesser and greater curvatures were enlarged and prominent. Several were removed from the lesser curvature. In view of the extensive involvement of the pylorus and prepyloric region and the extent of obstruction present, a gastric resection with a posterior Pólya anastomosis was performed.

The patient made an uneventful recovery except for a slight reaction following a blood transfusion of citrated blood given on the fourth postoperative day. He left the hospital on the seventeenth postoperative day, being asked to return in two to three weeks for further study, but he failed to do so and we were unable to trace him for seven months, when he returned to the hospital because of an injury to his back received by falling from the second floor while washing windows. The patient stated that he had gained 17 pounds in weight and was feeling quite well. He had to eat four to five times daily and could eat only a limited amount of food at one time.

A roentgenogram of the chest taken October 23, 1936, seven months after the operation (Fig. 2) was negative except for a few small areas of calcification in the left apex. A roentgenogram of the stomach (Fig. 3) revealed a well-functioning stomach. The

patient again left the hospital feeling quite well and when last seen, in December of 1938, was still gaining in weight and working at odd jobs.

Pathologic Examination.—Gross: The tissue received was a portion of a stomach including the pylorus, and measured 13 cm. in length and 10.5 cm. in circumference. The wall in the region of the pylorus measured up to 12 Mm. in thickness. The mucosa was deeply injected and the folds were flattened. Near the pylorus the mucosa presented a ragged, irregular defect (4.5 by 1.5 cm.) and involved most of the circumference. The ulcer was shallow and the floor was smooth and discolored purplish-tan. Nearby was a second smaller defect in the mucosa, star-shaped in appearance, which measured 3.5 by 1 cm. The remaining mucosa of the stomach was smooth and light purplish-gray. The

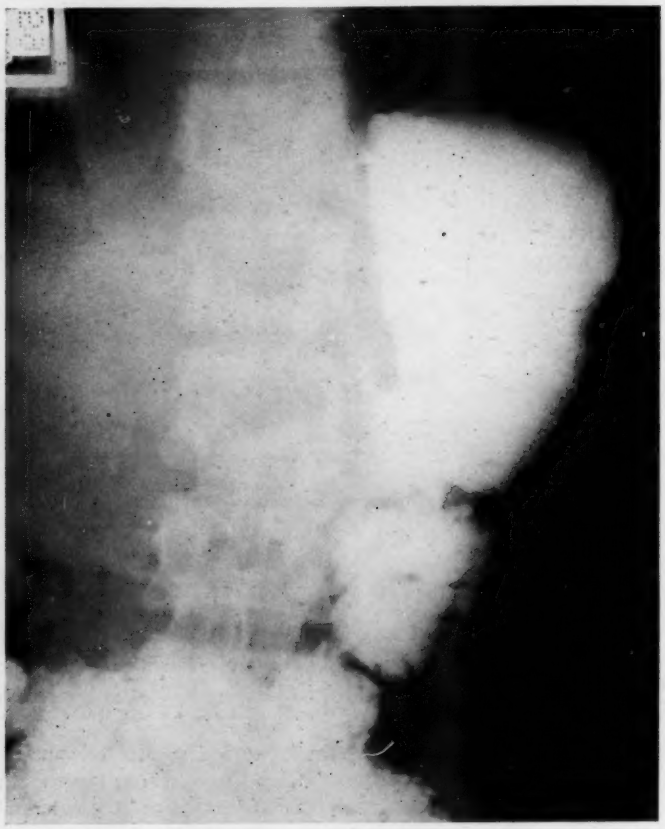

FIG. 3.—Roentgenogram of the stomach, seven and one-half months after partial resection, revealing a well-functioning stoma.

perigastric lymph nodes were enlarged, firm and measured up to 15 Mm. in diameter.

Microscopic.—Sections taken from the stomach revealed the ulcers to extend down into the submucosa. The floor was formed by a fibrinoid necrotic tissue which rested upon a very cellular and vascular granulation tissue. The granulation tissue consisted of numerous young capillaries, swollen fibrocytes, large mononuclear cells, round cells and scattered polymorphonuclear leukocytes. The underlying submucosa was markedly thickened, fibrosed and infiltrated by accumulations of lymphocytes, occasionally perivascular and in places tending to form lymph follicles (Fig. 4). In the region of the ulcer the muscularis propia was often interrupted by collections of lymphocytes, plasma cells, large mononuclear cells and single polymorphonuclear leukocytes. The muscle

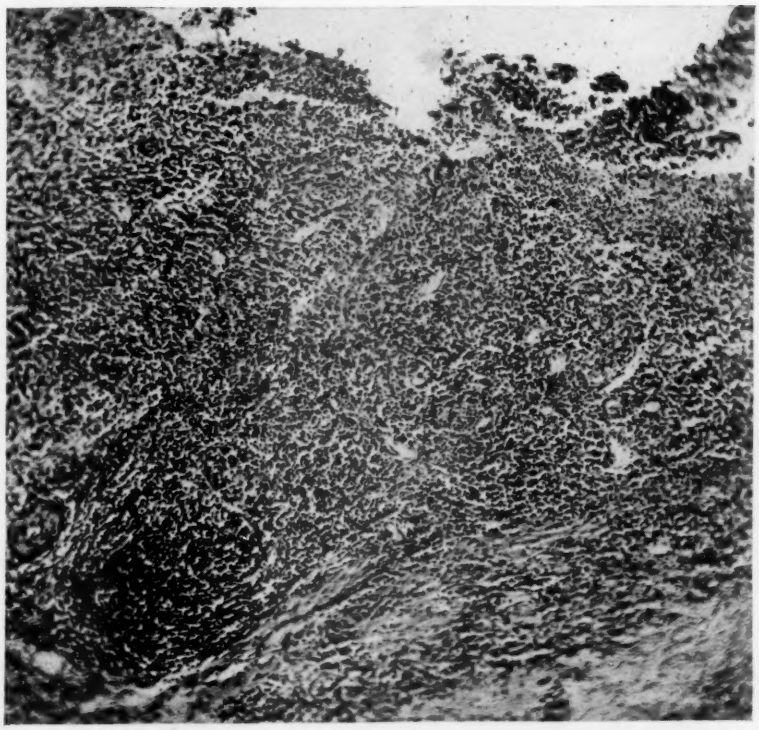

FIG. 4.—Photomicrograph of a section through one of the ulcers in the stomach. Note the nonspecific, inflammatory changes in the floor and the wall. (×100)

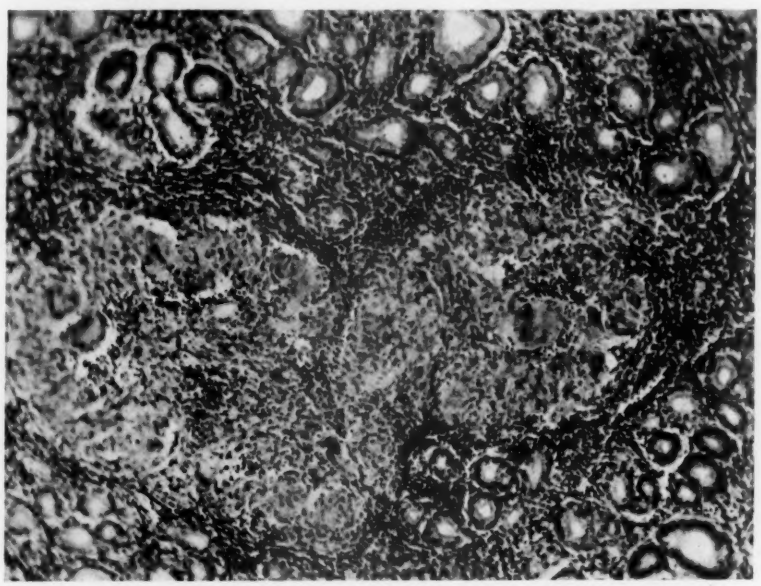

FIG. 5.—Photomicrograph of a section of the stomach showing two epithelioid cell tubercles with giant cells in the intact mucosa. (×150)

bundles in places were separated by a dense fibrillar connective tissue. The serosa was also thickened by a loose connective tissue in which were accumulations of small round cells, frequently present about large blood vessels. The mucosa adjacent to the ulcers was edematous, thickened, and scattered throughout were numerous small tubercles up to the size of a high power field composed of epithelial cells, lymphocytes, and single large multinucleated giant cells of the Langerhans type (Fig. 5). Occasionally the tubercles were fused together and surrounded by a dense collar of small round cells. The glands of the mucosa were frequently dilated and cystic. In the stroma, were accumulations of polymorphonuclear leukocytes, plasma cells and mononuclear cells.

The perigastric lymph nodes contained many epithelioid cell tubercles with giant cells of the Langerhans type (Fig. 6). The tubercles in some of the larger lymph nodes showed central necrosis. The sinuses were congested and the lymph follicles occasionally contained prominent germinal centers. Special stains, however, failed to reveal

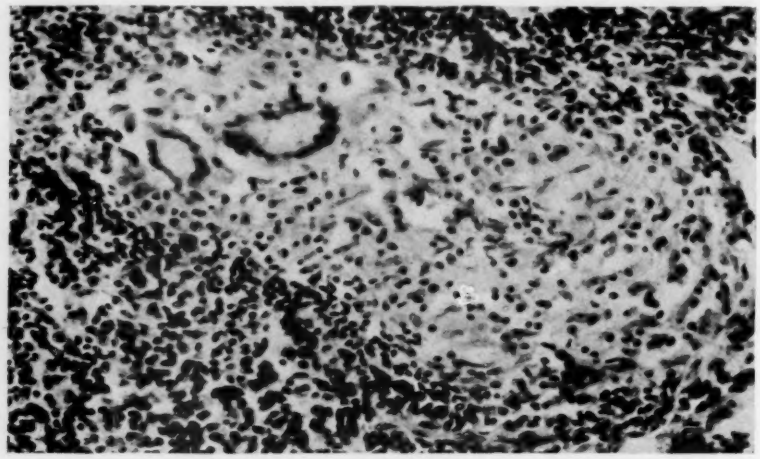

FIG. 6.—Photomicrograph of a section of one of the perigastric lymph nodes showing an epithelioid cell tubercle and several giant cells. (×300)

the presence of tubercle bacilli. *Pathologic Diagnosis:* Hyperplastic and ulcerative tuberculosis of the stomach involving the prepyloric and pyloric regions. Hypertrophic gastritis and hyperplastic tuberculosis of the perigastric lymph nodes.

Tuberculosis of the Stomach Without Clinical Manifestations.—The following three cases presented tuberculous changes in the stomach which were incidental findings during autopsy.

Case 1.—This case was a 38-year-old colored male, who died from an ulcerative pulmonary tuberculosis of the right upper lobe. In the stomach as well as in the ileum and cecum, there were numerous caseated tubercles that varied from pinhead to split-pea size. In the stomach the nodules were scattered along the lesser curvature of the mucosa.

Case 2.—A white woman, age 33, presented a caseous tuberculous adenitis of all lymph nodes and a caseous pleuritis. There were no evidences of tuberculosis in the lungs. The stomach presented geographic-like erosions especially about the cardia and fundus. They varied from 2 to 5 cm. in diameter and extended to the serosa. Over the serosa of the stomach were caseous material and loose fibrous adhesions.

Case 3.—This patient was a soldier, age 39, who died during the war from a chronic ulcerative tuberculosis of both lungs, associated with an ulcerative tuberculosis of the intestines and caseous tuberculosis of both kidneys. In the stomach, on the anterior wall 5 cm. below the cardia, a submucous caseous node was found which measured 16 Mm. in

diameter and was 6 Mm. high. Histologically, the node showed an extensive caseation necrosis, well circumscribed and confined to the submucosa. (This case was seen by the late Dr. R. H. Jaffé, who was kind enough to permit us to quote.)

Discussion.—Although tuberculosis of the stomach is usually seen by the pathologist at necropsy in cases of generalized tuberculosis, there remains a small number of cases in which tuberculosis manifests itself in the stomach as an isolated process. It is the latter type which is of interest to both gastro-enterologist and surgeon in view of the diagnostic problem that such a case presents. The differential diagnosis usually considered is either carcinoma or syphilis of the stomach and tuberculosis practically is never included. Even the gross examination of the excised segment of the stomach resembles a malignancy and the correct diagnosis is not suspected until microscopic examinations are made. The clinical course of tuberculosis of the stomach may resemble either a carcinoma or syphilitic process, while the roentgenologic studies favor the diagnosis of malignancy. The prognosis is usually very good following surgery in those cases in whom the general condition is often fairly good and when they have no signs of active tuberculosis elsewhere in the body. The case of Watson, Flint and Stewart[3] was of extreme interest in view of the fact that the tuberculosis had produced an hour-glass deformity and microscopically a complete metaplasia in the upper fundus was observed. The latter finding is also frequently seen in the mucosa of the bronchi in cases of pulmonary tuberculosis. In Baumgartner's[4] case, the tuberculous process in the stomach was coincidentally found with carcinoma.

Some investigators have considered the hyperplastic form of gastric tuberculosis as the primary source. This view is usually found to be incorrect, for at autopsy the primary source can often be traced to the lungs. In a series of 24 cases of gastric tuberculosis collected from the literature by Leriche and Mouriquand,[5] only two showed evidences of clinical tuberculosis in some other organ.

Males are usually more frequently affected than females—Melchior[6] gives the ratio of five to one; Grossman,[7] one to three, while Broders[1] gives it as two to one. It is three to four times more common in adults than children.

Microscopically, the stomach shows superficial ulcerations and a vascular, nonspecific granulation tissue. The histologic diagnosis of tuberculosis is confirmed when tubercles are present not only in the stomach wall, but also in the regional lymph nodes. The presence of tubercle bacilli cannot always be demonstrated.

The clinical picture reveals nothing characteristic. The earliest symptoms are those of chronic gastritis with loss of appetite and a sense of fulness or pressure in the epigastrium. This is followed by epigastric distress or pain of the ulcer type, loss of weight, and vomiting. The vomiting occurs late in the course of the disease and the vomitus is dark or suggestive of gastric hemorrhage. In Becker's[8] case, the tuberculosis was localized to the stomach

and caused a severe gastric hemorrhage. Diarrhea, if present, is usually due to ulcerations present in the small intestines. In about one-half of the cases a mass can be palpated in the epigastrium. A majority of the cases reported have also definite evidences of tuberculosis elsewhere in the body (Gualdi,[9] Olleros and Garcia,[10] *etc.*).

Laboratory data are not helpful in making a diagnosis, although the majority of cases reported reveal an absence or diminished amount of free acid. A hyperchlorhydria was found in the cases reported by Curschman[11] and Schlesinger.[12] Roentgenologic studies have been helpful in establishing the presence of an obstruction, but there is nothing characteristic about the nature of the defect or obstruction. In the majority of the cases reported, the roentgenologic diagnosis was carcinoma of the stomach—in others syphilis was suspected. The case of Walters, Kirklin, and Clagett[13] offered the same diagnostic difficulties that our case did, and only after histologic studies of the excised portion of the stomach was the tuberculous nature of the lesion recognized. Biopsy of a lymph node during life may be helpful in establishing a diagnosis, as shown in the cases of Lusena,[14] White,[15] and Melchior,[6] although they may be bacteriologically negative. In reviewing the reported cases, one finally comes to the conclusion that the clinical diagnosis of tuberculosis of the stomach cannot be distinguished from gastric ulcer or carcinoma, and in many respects the symptoms and pathologic findings closely resemble those of gastric syphilis.

In the treatment of tuberculosis of the stomach, a medical regimen has not proved of benefit. In a review of the surgical procedures performed, Lee[16] advises resection whenever possible in the chronic cases, and gastroenterostomy in acute cases and a subsequent resection later if the patient's condition warrants it.

SUMMARY

A case of a 34-year-old colored male, with tuberculosis localized to the stomach and perigastric lymph nodes, is described. Subsequent gastric resection has thus far produced complete eradication of the disease. Epithelioid cell tubercles were present in the gastric wall and in the perigastric lymph nodes.

The clinical and pathologic features of tuberculosis of the stomach are discussed.

One case of tuberculosis of the stomach was encountered in over 75,000 routine surgical specimens, while in a series of 554 cases of tuberculosis observed in 11,480 necropsies, two cases showed tuberculosis of the stomach as an incidental finding.

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LADD'S OPERATION FOR THE CURE OF INCOMPLETE ROTATION AND VOLVULUS OF THE SMALL INTESTINE PRODUCING DUODENAL OBSTRUCTION IN INFANCY*

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WHEN persistent vomiting in the early weeks of life yields bile stained material, a congenital obstruction in the duodenum must be considered; in this respect, at least, the lesion can be differentiated from hypertrophic stenosis at the pylorus which is associated with the return of colorless gastric contents. The type of congenital obstruction of the duodenum (*e.g.*, atresia, band, *etc.*) is usually difficult to demonstrate at the bedside and not infrequently even at operation. The many reports in the literature of congenital duodenal obstruction comprise a variety of lesions, many of them complicated in type. The three cases described herein, on the other hand, presented simple and similar clinical manifestations and anatomic findings and responded to relatively simple operative procedures. Because of this simplicity, the details of the experiences of these three patients are presented.

In 1932, Ladd[1] described 11 cases of congenital duodenal obstruction over half of which were identical with the three cases herein described. Ladd was able to find in the literature, only ten cases successfully treated. The obstruction was located in the terminal duodenum and upper end of the jejunum and was "extrinsic," being caused by congenital bands plus a twisting of the entire small intestine just below the ligament of Treitz. Inasmuch as the cecum lay in the upper left quadrant these cases represented incomplete rotation of the intestines as mentioned in greater detail below. In regard to the operative procedure he stated: "Though shocking, we feel that the only way to reduce the volvulus is by delivering the whole small bowel and untwisting it." Of the cases of malrotation which were operated upon, untwisting of the volvulus and cutting of bands was followed by cure in all; in one baby a gastro-enterostomy was performed with a fatal outcome. In a more recent report, Ladd[2] increased his series by 23, with 19 recoveries, and describes in more detail his operation for this (extrinsic) type of duodenal obstruction as a "transposing operation," emphasizing that reduction of the volvulus alone is not sufficient to permanently relieve the obstruction. The bands which impinge on the duodenum must be cut, thus allowing the cecum and ileum to be transposed toward their normal position in the right lower quadrant. Still more recently, Miller[3] cited a number of congenital obstructions but only a few were of the type herein described. McIntosh

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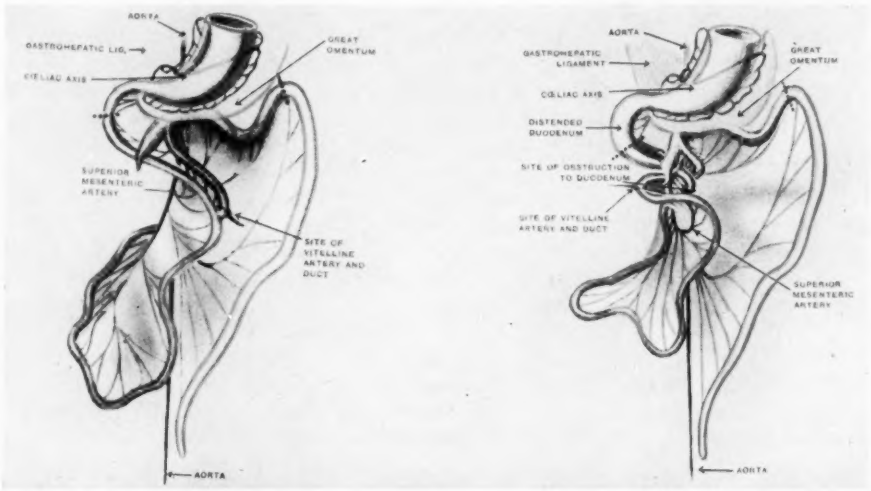
and Donovan[4] described a number of cases of disturbances of rotation, many quite similar to those of the extrinsic type described by Ladd and to those described herein.

Inasmuch as the important feature in these cases seems to be a disturbance in rotation, it appears important to refer to Dott[5] who, in 1923, presented a detailed discussion of malrotation with excellent charts illustrating three types of derangements corresponding to defects in the three stages of rotation. According to this description the present cases fell into the third group. Dott describes three of his own cases all of which died following operation; they presented much more complicated lesions than the ones herein described. Based upon the three stages of rotation the present cases would seem to be due to a failure of rotation only in the third stage, wherein,



A B

FIG. 1.—(A) represents arrested rotation of the third stage, and shows the close approximation of the ileum and upper jejunum with a slight twist of the prearterial segment through 90°. (B) represents a further step in the twist producing a volvulus of the entire small intestine. (Reproduced from Dott[5])

normally, the cecum and ileum leave their position in the upper left quadrant and continue in their rotation toward the right lower quadrant. When this stage is arrested the ileum (and cecum) remain attached to the jejunum and from this single point the entire small intestine hangs—thus enabling it to become twisted (Fig. 1). The twist or volvulus of itself is undoubtedly able to produce the duodenal obstruction although it is probable that the bands add to the completeness of the occlusion. The bands are also important in the pathogenesis in so far as they are attached to and fix the terminal ileum thus preventing the cecum and ileum from occupying their normal position in the right lower quadrant (Fig. 2).

CASE REPORTS

Case 1.—Hosp. No. N1972: Male, age 16 days. Since birth, there had been persistent bile stained vomiting; the weight dropped from seven pounds six ounces (3.3 Kg.)

to six pounds four ounces (2.8 Kg.). On admission, the general condition was good but the next day he suddenly became listless, the skin dry and inelastic. A diagnosis was made of duodenal obstruction and an operation performed. Through a right rectus incision, a tremendously dilated duodenum was found. The entire small intestine was collapsed and the cecum and appendix were found in the left upper quadrant. A twist, just distal to the ligament of Treitz, was found involving all of the small intestine; this was corrected by rotating the entire small intestine in a counter-clockwise direction. The ligament of Treitz could not be explored sufficiently because of the patient's poor general condition, which necessitated an immediate termination of the operation. On return to the ward the patient was in shock but recovered completely with the administration of fluids and a transfusion. On discharge, the patient was taking feedings well, and gaining in weight.

At five months of age the patient was admitted a second time because of recurrence of vomiting which ceased on thickened feedings. Roentgenologic examination showed no obstruction and a barium enema canalized to the hepatic flexure.

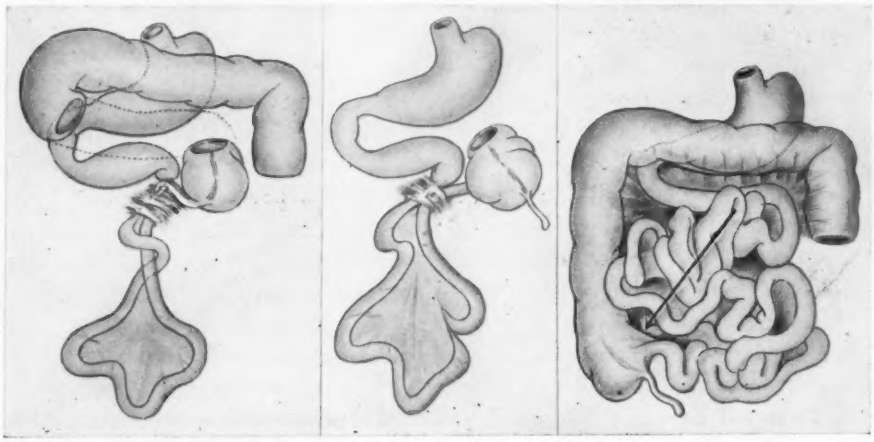
Two weeks later patient was admitted for a third time, with a history of persistent vomiting of several days' duration. A roentgenogram showed a complete obstruction at the terminal duodenum. A second operation was carried out; this time an upper left rectus incision was employed. The small intestine was eviscerated and found to be twisted as at the previous operation. The volvulus was reduced by untwisting the intestines in a counter-clockwise direction. The mesentery was the site of a tremendous edema. At the hepatic flexure the transverse colon turned sharply on itself so that the cecum lay in the upper left quadrant. The ileum was then found lying along the beginning jejunum and attached to it by well developed fibrous bands. These were severed, whereupon it became possible to return the cecum and terminal ileum toward the right lower quadrant. After division of the band, a definite groove could be seen at the beginning jejunum above which the duodenum was tremendously dilated. Recovery was entirely uneventful, and the patient remained well up to the present time (two years).

Case 2.—Hosp. No. 02129: Female, age 1 month. There was a history of bile stained vomiting during the first 12 days of life, no vomiting for the next week, but persistent vomiting since. On admission, the baby was prostrated, dehydrated and exhibited convulsive movements during which she became quite cyanotic. Rectal bleeding was also observed. A roentgenogram following the ingestion of a barium meal showed a characteristic picture of obstruction at the terminal duodenum. The general condition of the patient was only slightly improved by conservative measures, and two days after admission operation was performed, employing local followed by general anesthesia. An upper left rectus incision was made; the cecum was found in the upper left quadrant with the appendix curled around the beginning jejunum. The entire small intestine was collapsed; it was eviscerated and a twist found and corrected by rotation in a counter-clockwise direction. No cause was found for the rectal bleeding except the volvulus. The general condition of the patient did not permit an adequate dissection of the ligament of Treitz, and the abdomen was closed. The change following the operation was spectacular; the color improved, breathing became more regular, the cry vociferous. The patient was discharged 12 days later, having gained one pound nine ounces (700 Gm.).

At six weeks of age, the patient was admitted a second time and the feeding formula was adjusted. The baby remained well for one month, when she was readmitted for a third time, with a history of an occasional vomiting until two days before admission when she vomited everything. She was treated conservatively for one week, when it became obvious that the obstruction had recurred. A second operation was undertaken through the same upper rectus incision. A large postoperative band was found occluding the jejunum. There was also a recurrence of the twist. Exploration at the ligament of Treitz did not seem to reveal any obstructing band, and the abdomen was closed without doing anything further. The patient was discharged entirely well, with no further

vomiting, and remained well for another month, during which time she gained two pounds (1 Kg.) in weight.

The patient was admitted a fourth time because of multiple furuncles about the head, which were treated and healed in about three weeks. Just before she was about to be discharged she suddenly developed persistent vomiting, and roentgenologic examination showed a recurrence of the obstruction at the terminal duodenum. The general condition of the patient was excellent at this time. A third operation was carried out through the old upper rectus incision; the small intestine was eviscerated and found to be slightly distended, unlike its previous appearance. The mesentery was edematous and lymph nodes tremendously engorged. Visible lymph had accumulated beneath the peritoneum and had extended up the ligament of Treitz. Several bands were producing partial obstruction but upon careful exploration of the beginning of the jejunum it was apparent that an intermittent volvulus had been responsible for most of the changes noted. Further dissection revealed definite congenital bands between the beginning of the jejunum with the terminal ileum which had not been severed at the previous operations.



A B C

FIG. 2.—Diagrammatic sketches from the findings in Case 3:
(A) Note the dilatation of the duodenum above the bands and the volvulus which has been partly untwisted.
(B) The volvulus has been entirely reduced and the bands are ready to be cut.
(C) The bands have been cut and the cecum replaced toward the right lower quadrant in the direction indicated by the arrow.

These bands were cut extensively up to the point where the dilated duodenum became suddenly constricted. This resection permitted replacement of the cecum toward the right lower quadrant aided by the rotation of the entire small intestine in a counter-clockwise direction. Recovery from this operation was uneventful and patient has remained entirely well (one year).

Case 3.—Hosp. No. 0859: Male, age 5 days. There was a history of persistent bile stained vomiting since birth. A roentgenogram, following the ingestion of a barium meal, revealed a characteristic obstruction at the terminal duodenum. The patient was treated conservatively for seven days and then operated upon, under general anesthesia, through an upper left rectus incision. The entire small intestine was collapsed but twisted; it was eviscerated and rotated in a counter-clockwise direction. The upper left quadrant was then carefully explored. The cecum lay in close relationship to the ligament of Treitz, the appendix being curled around the beginning of the jejunum. A band was found binding the jejunum to the ileum. This was cut extensively, until the dilated duodenum was reached. After this it was possible to mobilize the cecum and partially

replace it in the right lower quadrant (Fig. 2). The abdomen was closed and recovery was uneventful. There has been no further vomiting since operation (one year).

Discussion.—Very little can be added to the clinical description and operative treatment recorded by Ladd.[1, 2] From the cases herein reported, as well as from those described by Ladd, one may say that incomplete rotation with volvulus produces manifestations which can be readily recognized and readily corrected.

The most important symptom produced by such a lesion is persistent bile stained vomiting, beginning shortly after birth but in some cases interrupted by periods during which all food is normally retained. Undoubtedly, this is possible because the twist in the intestines may become spontaneously, though only temporarily relieved. During periods of obstruction visible gastric peristalsis may be seen passing from left to right, just as is true in pyloric stenosis. If the baby is examined roentgenologically, no dilated loops of intestine are to be seen but a dilated stomach and duodenum can often be identified; if barium is given by mouth the shadows cast by the stomach and duodenum are clear and characteristic. Significant, too, is the absence of general abdominal distention; the fulness in the upper abdomen can be made to disappear on aspiration by lavage of the gastric and duodenal contents.

The general manifestations of dehydration are produced if vomiting is sufficient to result in anhydremia. In addition to this, attacks of prostration and listlessness may occur similar to those seen in intussusception. This is doubtless due to circulatory changes produced by an especially severe twisting or volvulus. In one of the present cases passage of blood per rectum occurred, suggesting, too, circulatory obstruction produced by the volvulus.

Once the diagnosis is made, unless signs promptly disappear, celiotomy is indicated. General anesthesia and an adequate incision are necessary. An upper left rectus approach leads most readily to the ligament of Treitz which is the seat of the lesion. Much time is saved and unnecessary intraperitoneal trauma avoided by prompt evisceration of the entire small intestine. Though, at first consideration, this procedure seems to be too radical, the advantages gained far outweigh the moderate shock it undoubtedly produces. In the first place, evisceration is really essential in order to untwist the volvulus by rotation in a counter-clockwise direction. In the second place, evisceration permits adequate exposure of the ligament of Treitz, which is necessary in order to sever the bands obstructing the terminal duodenum and the upper jejunum. Moreover, since these bands are also attached to the terminal ileum, by dividing them it becomes possible to mobilize the cecum and ileum, releasing their fixation to the upper left quadrant and allowing them to be placed toward their more normal position in the right lower quadrant. On the basis of the present observations (Case 2) this is essential in order to prevent recurrence of the volvulus. Gastro-enterostomy is unnecessary in this type of obstruction and if carried out adds to the risk of the operation.

SUMMARY.—Three cases are described of duodenal obstruction in infancy, due to volvulus of the entire small intestine, plus congenital (extrinsic)

bands occluding the terminal duodenum and upper jejunum. The defect seems to be a failure in the third stage of intestinal rotation associated with an attachment of the terminal ileum to the upper jejunum in the upper left quadrant. Recovery followed in all three cases after carrying out Ladd's operation, *i.e.*, untwisting the volvulus plus cutting the extrinsic bands attached to the upper jejunum and terminal ileum.

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PLASMA TRANSFUSION IN EXPERIMENTAL INTESTINAL OBSTRUCTION

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WE have recently published[1] evidence that in experimental intestinal obstruction plasma is lost to an extent sufficient in itself to cause death. Most of this plasma loss is attributable to the factor of distention alone. Some loss of plasma due to dehydration occurs during the course of the experimental period but it is not of sufficient magnitude to be significant in the death of the distended animal. Previous studies[2, 3] showed that loss of blood, fluid and electrolytes into the intestinal lumen, bowel wall, and peritoneal cavity was not responsible for the plasma loss or for the rapid death from obstruction with distention. The possible deleterious influence of noxious nerve stimuli originating in the distended bowel was also excluded from responsibility. Furthermore, it was found that animals whose empty small intestines were obstructed and distended did not survive as long as others which were obstructed but not distended, and that the survival time was shortened in proportion to the height of the intra-intestinal pressure. The one uniform finding which constituted an adequate explanation for the quicker death of the distended animals was a progressive and extensive loss of blood plasma.

We have, to date, no conclusive answer as to the mechanism by which distention produces plasma loss, although our studies suggest that part of the plasma is forced into the interstitial spaces of the pelvis and lower limbs because of impeded venous return from these areas. In any case the obvious inference from these observations, if they are correct, is that transfusions of plasma, in sufficient volume to replace the plasma which is lost, should have a favorable influence upon the course of the process. In this communication are described the results of experiments designed to elucidate this question.

Method.—Dogs were used exclusively. Their normal plasma and whole blood volumes were determined under intraperitoneal nembutal anesthesia immediately preceding or several days in advance of the experiment by a technic already described.[1] After 24 hours of starvation, but with water allowed, the dogs were anesthetized by intraperitoneal nembutal. The pylorus was ligated and the ileocecal valve was divided, its distal end inverted

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and a glass cannula tied into its proximal end. The cannula was brought out through a stab wound after closing the abdominal incision and connected to a Perusse pressure bottle. The entire small intestine was kept continuously inflated with air at a pressure of 20 cm. of water (a level consistent with that observed in clinical and experimental obstruction) until death occurred.

Plasma for transfusion was obtained from large, normal, healthy dogs by exsanguination under sterile precautions. Fifty cubic centimeters of a sterile 25 per cent sodium citrate solution in physiologic saline was added to each 450 cc. of blood and stored for from one to three days at a temperature varying from 0 to 4° C. Before use the supernatant plasma was siphoned off and diluted to two or three times its volume with physiologic saline to reduce its viscosity so that it would run without clotting. Some of the specimens used showed a slight hemolysis.

Immediately after obstructing and distending the intestine, plasma (plus two to three times its volume of physiologic saline) was run into the femoral vein at a rate of five to eight drops per minute until its administration was purposefully interrupted or until the supply was exhausted or until the animal died. The volume transfused in a given time differed from one animal to another in accordance with the calculated loss in plasma volume to be anticipated.

Determinations of plasma and whole blood volumes were made at intervals as convenience and the circumstances of the experiment allowed.

In order to determine the specific value of plasma as against other fluids which are considered useful for restoration of lost fluid, intravenous physiologic saline (in one experiment 6 per cent acacia [Lilly] was added) was given to different dogs and its effect on plasma volume and survival time noted.

The details of each experiment are listed in Table I. The significance of the results can best be appreciated by discussing each experiment individually.

DOGS RECEIVING PLASMA TRANSFUSIONS

Experiment I.—This dog received plasma continuously from the beginning of the experiment until the thirty-ninth hour of distention. Death occurred five hours after the plasma was discontinued. The total survival time of 43 hours is in contrast to an average survival time of 20.8 hours for distended dogs not receiving plasma.[1] Two hundred cubic centimeters of plasma was given during the first five hours, with a resultant increase of 7 per cent in plasma volume instead of an expected average fall of 35 per cent after a similar interval of distention in dogs not receiving plasma. There was a simultaneous decline in total blood volume of 6 per cent because of a 15 per cent loss in red cell volume, which is presumably, at least in part, a relative rather than an absolute loss. Distended dogs not receiving plasma uniformly show a rise in hematocrit averaging 37.8 per cent after four to six hours, but this dog showed a fall, also relative, of 12 per cent. An additional 250 cc. of plasma was administered by the end of the twenty-third hour of distention. The fall in plasma volume at this time was 3 per cent in contrast to an average fall, after approximately the same interval, of 55 per cent in distended dogs not receiving plasma. After the thirty-eighth hour, by which time the dog had received a total of 650 cc. of plasma (plus the diluent of 1,300 cc. of physiologic saline), the plasma transfusion was stopped. Death occurred five hours later.

COMMENT.—In a previous series of 11 dogs with obstruction and distention but no plasma transfusion, seven died in 20 hours or less. The longest survival time was 30 hours. The fall in plasma volume in those dogs surviving as long as 23 hours was never less than 45 per cent, an amount sufficient to cause death. Since the fall in Dog I of the present series after this interval was only 3 per cent, we conclude that plasma transfusion was responsible for prolonging the survival time to approximately twice the average in those dogs which did not receive plasma.

Experiment II.—After 20 hours of obstruction and distention during which 350 cc. of plasma was infused, the plasma volume increased 3.2 per cent and the hematocrit fell 16 per cent, results which are substantially the same as in Experiment I. An additional 150 cc. of plasma was administered during the next 16 hours, but, unfortunately, a plasma volume measurement was not obtained until six hours after the plasma was discontinued (because of exhaustion of supply). During this interval of distention without plasma replacement a 39 per cent fall in plasma occurred and the dog died 14 hours later, with a total survival time of 56 hours, which is not far removed from the expected survival time of an intact dog under continuous intraperitoneal nembutal anesthesia.[1] Had the cannula in the ileum not perforated the wall of the intestine by mechanical friction, with resulting terminal, extreme pneumoperitoneum, the survival time might have been even more prolonged.

COMMENT.—It will be noted that the total volume of the transfused plasma exceeded the dog's own plasma volume. In spite of this a 39 per cent loss of plasma occurred within six hours after the plasma transfusion was discontinued.

It is apparent from this experiment that the plasma loss caused by distention continues uninterruptedly so long as distention is maintained, and that the plasma infused serves only to replace what is lost. Evidence is available that slowing or reversal of the process by which plasma is lost can be achieved by decompressing the intestine.[4] If, while distention persists, the plasma loss proceeds at a rate exceeding that of replacement, the fall in plasma will go on to cause a fatal issue. This is indicated in Experiment III.

Experiment III.—The original plasma volume of this dog was 656 cc. According to our previous data the expected loss from distention in four to six hours would equal 229 cc. Only 75 cc. was transfused during the first seven hours and a fall of 30 per cent in plasma volume was observed. At this rate of plasma loss the animal's survival time would hardly have reached its actual value of 46 hours. We attribute this survival period to the fact that an additional 225 cc. of plasma was administered between the seventh and the thirtieth hours. Death occurred six hours after plasma administration was stopped.

The effect of supplying plasma in excess of the expected calculated plasma loss is illustrated in the next experiment.

Experiment IV.—In this dog, with an initial plasma volume of 517 cc., the expected loss after four hours without plasma transfusion would be 181 cc. Two hundred cubic centimeters of plasma was administered with a resulting gain in plasma volume of 10 per cent. The hematocrit fell 20 per cent. Without plasma transfusion an increase in the hematocrit of some 45 per cent would be anticipated. Similarly, after 23 hours, when a total of 500 cc. of plasma had been given (216 cc. more than the average expected loss when plasma is not transfused), a 19 per cent increase in plasma volume and a 31

per cent decrease in hematocrit were observed. (In this, as in one other distended animal receiving plasma, urine was excreted during the experiment and the tissues were slightly edematous at autopsy.) Although an additional 100 cc. of plasma was administered during the next ten hours, the dog died after 43 hours, surviving only nine hours after the plasma transfusion was interrupted.

COMMENT.—It is apparent, therefore, that when plasma is administered in adequate quantity it serves to sustain the distended dog while it is being administered and for a variable, but only short interval afterward. It should not be surprising that the survival time is not longer, if one bears in mind that in addition to the deteriorating effect of the continuing loss of plasma, the limit of survival of an intact dog under continuous intraperitoneal nembutal anesthesia is being approached.[1]

Further evidence that plasma continues to be lost so long as distention is maintained may be observed in Experiment V.

Experiment V.—One hundred cubic centimeters of plasma was transfused during the first five hours of distention. This quantity is insufficient to balance the expected calculated loss of about 297 cc. (35 per cent of 894 cc.). Consequently a drop in plasma volume of 16.4 per cent was observed after the fifth hour. During the next nine hours 300 cc. more of plasma was administered in order to approximate the expected total calculated loss (400 cc.) after 14 hours of distention. The plasma infusion was then stopped and seven hours later, or 21 hours after the onset of the distention, the plasma volume had fallen only 6.4 per cent below its value after the fifth hour, which clearly demonstrates the sustaining function of the infused plasma. But in a further six hours the plasma loss had reached 47.9 per cent, with death following nine hours later, a total survival time of 36 hours.

COMMENT.—We consider that this death occurred six hours earlier than the next earliest death in this group of five animals because the plasma transfusion was given for only 14 hours instead of for 33 or more hours as in the other four dogs.

The data in the next two experiments are incomplete, but are of value in connection with the general thesis of this paper.

Experiment VI.—The changes in plasma volume in this dog could not be measured because the donor's plasma had been partly diluted with distilled water which caused marked hemolysis. This prevented photo-electric colorimetric determinations of plasma volume. In spite of the hemolysis, the presence of severe strangulation of the bowel, and a terminal pneumoperitoneum due to rupture of the bowel by the glass cannula,* the dog survived 38 hours, having received 400 cc. of plasma during the first 19 hours.

COMMENT.—This is in marked contrast to the survival time of ten, 12 and 18 hours, respectively, of a previously reported group of three dogs with venous strangulation and distention, but no transfusion of plasma.[1]

Experiment VII.—A week before the experiment this dog's control plasma volume was 994 cc., but when the experiment was started the dog was very sick. Upon opening the abdomen, generalized peritonitis was found. He was, nevertheless, distended for four and one-half hours, during which time he did not receive plasma. At the end

* We subsequently learned to prevent this by using, instead of an ordinary glass tube with an open end, a cannula with a balloon tip containing numerous perforations.

TABLE I

THE EFFECT OF CONTINUOUS INTRAVENOUS INFUSION OF PLASMA UPON THE SURVIVAL TIME, THE PLASMA AND WHOLE BLOOD VOLUME, AND THE HEMATOCRIT IN DOGS WITH CONTINUOUS DISTENTION OF THE ENTIRE SMALL INTESTINE AT A PRESSURE OF 20 CM. OF WATER

Dog No.	Weight (in Kilos)	Survival Time (in Hours)	Hours After Beginning Distention	Total Cumulative Volume of Infusate (in Cc.)	Plasma Volume (in Cc.)	Change in Plasma Volume (in Per Cent)	Total Blood Volume	Change in Total Blood Volume (in Per Cent)	Red Cell Volume (in Cc.)	Change in Red Cell Volume (in Per Cent)	Hematocrit (in Per Cent)	Change in Hematocrit (in Per Cent)	Plasma Total Red Volume. Blood Cell Volume (in Per Cent of Body Weight)			Remarks
1	16.8	43	0		705		1,639		934		57.0		4.2	9.7	5.5	
			5	200	755	+ 7.0	1,540	− 6.0	785	−15.0	50.0	−12.0	4.5	9.1	4.6	
			23	450	680	− 3.0	1,402	−14.0	722	−22.0	51.5	−11.0	4.0	8.4	4.4	
			38	650												
2	9.5	56	0		451		902		451		50.0		4.7	9.4	4.7	Severe pneumoperitoneum at autopsy
			20	350	466	+ 3.2	804	−10.0	338	−25.0	42.0	−16.0	4.9	8.4	3.5	
			36	500												
			42		276	−39.0	613	−32.0	371	−18.0	55.0	+10.0	2.9	6.5	3.6	
3	14.4	46	0		656		1,339		683		51.0		4.6	9.3	4.7	Distention started 12 hours after obstruction, without distention
			7	75	458	−30.0	904	−32.0	446	−34.0	51.5	0.0	3.2	6.3	3.1	
			38	300												
4	16.1	42	0		517		1,229		712		58.0		3.2	7.6	4.3	
			4	200	575	+10.0	1,064	−11.0	489	−31.0	46.0	−20.0	3.5	6.6	3.1	
			23	500	718	+19.0	1,197	− 1.0	479	−34.0	40.0	−31.0	4.3	7.3	3.0	
			33	600												
5	17.5	36	0		849		1,439		590		41.0		4.8	8.2	3.4	
			5	100	709	−16.4	1,266	−12.0	557	− 5.5	44.0	+ 6.4	4.0	7.2	3.2	
			14	400												
			21		654	−22.9	1,257	−12.6	603	+ 2.1	48.0	+11.5	3.7	7.1	3.4	
			27		442	−47.9	945	−34.5	503	−14.0	53.0	+22.6	2.5	5.7	3.2	
6	11.8	38	0													Venous strangulation of intestine; pneumoperitoneum; hemolyzed blood
			19	400												
7	18.1	23½	0		994?		1,713?		719?		58.0?		5.4?	9.4?	4.0?	Peritonitis at beginning of experiment. In extremis at the end of five hours of distention. Plasma infusion started at that time
			4½		620	−37.0?	1,140	−33.0?	520	−26.0?	46.0	−20.0?	3.4?	6.3?	2.9?	
			23	250	718	−27.5?	1,408	−22.0?	790	+ 9.0?	49.0	−15.0?	3.9?	7.7?	3.8?	

of this interval he appeared moribund. Although the resulting drop in plasma volume of 37 per cent is about what may be expected in an animal without peritonitis, it is an unreliable determination because the initial control volume was probably quite different from the value obtained a week previously. But it was used as a base line for the determination of subsequent changes.

The animal then had 100 cc. of plasma in physiologic saline administered rapidly, with immediate and marked improvement in his general condition. Plasma was continued intravenously for the next 18½ hours, when he died, having received a total of 250 cc. of plasma. The plasma volume shortly before death had been increased some 16 per cent above the level prevailing after four and one-half hours of distention.

COMMENT.—The rapid deterioration caused by the first four and one-half hours of distention is suggestive of the clinical experience that distention seriously increases the burden of peritonitis. The prolongation of life for 18 hours after what were, apparently, terminal respiratory efforts demonstrated the protective effect of plasma transfusion.

DOGS RECEIVING INTRAVENOUS SALINE

It will be recalled that in all of the experiments described the plasma was transfused after having been diluted with two or three volumes of physiologic saline in order to permit the plasma to run smoothly and uniformly without clotting. From earlier data, previously reported, we were convinced that dehydration and dechlorination were not substantial factors in the early death of dogs obstructed and distended in accordance with our technic. To further substantiate this belief, and to show whether or not there was any protective virtue in the physiologic saline administered with the plasma in the experiments with which we have been here concerned, five dogs were treated with physiologic saline alone. In Experiments VIII, IX and X (Table II) physiologic saline injections were administered in amounts and at rates equivalent to those given with plasma in Experiments I to VII (Table I). In Experiments XI and XII, 500 cc. was injected rapidly at the end of the fourth and thirteenth hours of distention, respectively. The average survival time in these five dogs was 15.8 hours, which is in contrast to 43.5 hours for the first six dogs of this series receiving plasma and saline, but quite comparable to the average survival time (20.8 hours) of dogs receiving no plasma or saline.

This amply confirms our previous conclusion that dehydration and dechlorination were not significant factors in the death of our distended animals, and shows that physiologic saline exerts little or no protective effect. We are in agreement with others (Taylor, Weld and Harrison[5]) who believe that when and if dechlorination occurs in the course of intestinal obstruction, it is an incidental factor which deserves correction, but is by no means a crucial factor in the lethal effects of obstruction.

In one experiment with 6 per cent acacia added, no protection was afforded the animal, as judged by the survival time (Table II).

Discussion.—The fact that distention is the central disturbing feature of uncomplicated intestinal obstruction is universally accepted. It is also gener-

TABLE II

THE EFFECT OF CONTINUOUS INTRAVENOUS INFUSION OF PHYSIOLOGIC SALINE UPON THE PLASMA AND BLOOD VOLUME, HEMATOCRIT AND SURVIVAL TIME OF DOGS WITH INTESTINAL OBSTRUCTION AND CONTINUOUS DISTENTION OF THE ENTIRE SMALL INTESTINE AT A PRESSURE OF 20 CM. OF WATER

Dog No.	Weight (in Kilos)	Hour After Beginning Distention	Type and Amount of Solution Given (in Cc.)	Survival Time (in Hours)	Plasma Volume (in Cc.)	Reduction in Plasma Volume (in Per Cent)	Total Blood Volume (in Cc.)	Reduction in Total Blood Volume (in Per Cent)	Red Blood Cell Volume (in Cc.)	Change in Red Blood Cell Volume (in Per Cent)	Hematocrit (in Per Cent)	Remarks
8	18.2	12	Saline 750	12								
9	14.1	14	Saline 550	14								
10	18.0	0			665		1,279		614		48	Venous strangulation of entire small bowel
		12	Saline 800	15	382	43.0	1,009	21.0	627	+2.0	62	
		15	Saline 1,100									
11	23.6	0	Saline 500	18	1,090		2,180		1,090		50	Saline given in single dose instead of continuously after fourth hour of distention
		4			724	33.5	1,810	16.9	1,086	0.0	60	
12	11.0	0	Saline 500	20	655		1,101		446		41	Saline given in single dose instead of continuously after the thirteenth hour of distention
		13			358	45.3	745	32.3	387	−13.2	52	
13	14.5	0	6% acacia in saline 300	11½								
		11½										

ally agreed that the correction of dehydration and electrolytic imbalance do not prevent death, and that death may occur before starvation becomes a significant factor, and before strangulation or peritonitis supervenes.

We[1] have recently provided data to show that a fatal loss of plasma occurs as a direct consequence of increased intra-intestinal pressure, and that this plasma loss is independent of the loss of fluid or electrolytes into the intestinal lumen or wall or into the peritoneal cavity. Evidence was already at hand to show that the survival time of distended animals is inversely proportional to the height of the intra-intestinal pressure. We believe that this is due to a more rapid loss of plasma in animals with higher intra-intestinal pressures.

We do not insist that the loss of plasma is the only significant phenomenon in the lethal process. But it is the only one brought forward, thus far, which may be regarded as of basic importance. For, obviously, even if other primary mechanisms should in time come to be shown as operative in the death from intestinal obstruction, their circumvention will not substantially alter the course of the process so long as the plasma loss remains uncompensated.

The validity of the foregoing experimental observations on the therapeutic effect of plasma transfusions in intestinal obstruction and distention rests on the significance of the prolongation of the survival time from an average of some 20 hours to one of 40 or more. If plasma loss is the crucial factor, why should its replacement postpone death for only 40 or 50 hours; why not indefinitely? The answer is twofold: (1) The plasma transfusion was not continued until death occurred; it was interrupted six or more hours before death, and during this interval a sharp drop in plasma volume occurred. Had plasma replacement been carried on there is reason to believe that the survival time would have been even longer. (2) There are limitations on the survival time of an animal which must, in the nature of the experiment, be kept lying on its back continuously under the constant influence of an anesthetic. The survival time of an intact dog under these circumstances is a matter of some two to three days. Such a dog dies without a serious loss in plasma volume so that, presumably, transfusion of plasma would not prolong life significantly. It would be illogical to expect that the infliction of a still greater burden, even though to a large extent nullified, should permit survival for as long a period of time. Hence, we believe that the considerably longer period of survival achieved by plasma replacement is of primary significance and confirms our contention that the loss of plasma is a vital characteristic of the process of decline in intestinal obstruction.

SUMMARY.—Five dogs subjected to intestinal distention at a pressure of 20 cm. of water had plasma administered continuously, intravenously, to replace part or all of the anticipated loss of plasma as determined from previous data already published. Effective maintenance of the control plasma volume occurred when the supply of intravenous plasma was adequate. Interruption of the administration of plasma was followed by a drop in plasma volume sufficient to cause death. The survival time of these dogs was prolonged from

an expected average of 208 hours for distended dogs not receiving plasma, to 40 or more hours.

The duration of life of similarly distended dogs which received intravenous physiologic saline but no plasma was not prolonged beyond the survival time of dogs receiving nothing parenterally. The survival time of one dog, which received acacia solution in saline, was about the same as that of dogs receiving saline alone.

CONCLUSIONS

(1) The intravenous injection of plasma, in amount adequate to replace that lost as a result of obstruction and distention of the empty small intestine, confers a protective influence sufficient to markedly prolong the life of the animal.

(2) The intravenous injection of physiologic saline, in amount sufficient, or more than sufficient to replace fluid lost under the conditions of our experimental technic, confers no noticeable benefit.

(3) Loss of plasma continues so long as distention continues in the obstructed small intestine of the dog. The extent of this loss, if uncompensated, is sufficient in itself to cause death, and is of primary importance in the pathologic physiology of intestinal obstruction.

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METASTATIC PULSATING TUMOR OF BONE SECONDARY TO RENAL CARCINOMA

CASE REPORT

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ADENOCARCINOMA, popularly known as "hypernephroma" or "Grawitz tumor," is the most common form of renal carcinoma. It is generally conceded that such tumors tend to metastasize to the osseous system. In a series of 63 cases, Geschickter and Copeland[1] found 22 instances, or 35 per cent, of skeletal metastases. The bones most frequently involved in the order of frequency were: The humerus, spine, femur, pelvis, ribs, bones of foot, skull and sternum. The incidence of skeletal metastases in renal carcinoma, as observed in different clinics, is listed in Table I. Certain interesting features of an instance of this condition, recently observed in the Urologic Service of the Peiping Union Medical College Hospital, warrant this report.

TABLE I

INCIDENCE OF SKELETAL METASTASES IN RENAL CARCINOMA AS OBSERVED IN SEVERAL CLINICS

Author	Clinic	Hypernephroma No. of Cases	Skeletal Metastases No. of Cases	Skeletal Metastases Per Cent
Geshickter and Copeland[1]	Johns Hopkins Hosp.	63	22	35.0
Garceau[2]	Mass. Gen. Hosp.	176	35	20.0
Dresser[3]	Mass. Gen. Hosp.	46	6	13.0
Judd and Hand[4]	Mayo Clinic	367	11	3.0
Diez and Michans[5]				50.0
Shih and Wang	P. U. M. C.	14	3	21.4

Case Report.—M. C. Y., a Chinese male, age 68, was admitted to the hospital, in May, 1938, complaining of a painful swelling of the right wrist. He had first noticed a small, firm and painless swelling over the ulnar side of the right wrist in January, 1938. Intense pain developed when he attempted to reduce this mass by massage. The pain was constant and throbbing in character, and was aggravated by motion of the wrist. The dorsum of the hand became swollen soon afterward and the motion of the wrist became limited on account of the pain and edema. The tumor gradually increased in size and was observed to be pulsating from the time of the onset of the pain. In April, a similar tumor appeared in the left occipital region. It was moderately painful, definitely pulsating and slowly increasing in size. The patient's appetite was impaired and there was much loss of weight.

Only by careful review of the past history was it possible to disclose the fact that, in September, 1937, the patient had been seized by severe throbbing pain in the right upper abdomen which lasted throughout one night and was relieved by gentle massage. At the

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same time a small, firm mass was first noticed in the right hypochondrium, which has persisted. The patient had three subsequent attacks of milder pain. There were no urinary symptoms except "hematuria" which had been present for several months ten years previously, and had recurred in a milder form shortly before admission.

Physical Examination.—The patient's general condition was fair. The abdomen was found to be bulging in both flanks and shifting dulness was easily demonstrated. Under the costal margin, a firm, tender mass, about 10x10 cm., could be palpated in the region of the right kidney (Fig. 1). This mass was not fixed but moved with respiration. The right hand was warmer than the left and its superficial veins were dilated. The distal end of the forearm was definitely enlarged, especially on the ulnar side (Fig. 2). The circumference of the wrist at the level of the styloid process of the radius was 20.5 cm. on the right and 17.0 cm. on the left side. The swelling measured 11x8 cm. and felt cystic in some areas. All over this mass, expansile pulsation, synchronous with the heart beat, could be felt and a loud systolic bruit was audible. Flexion of the wrist and interphalangeal joints, pronation and supination of the forearm were much limited. Another cystic

FIG. 1. FIG. 2. FIG. 3.

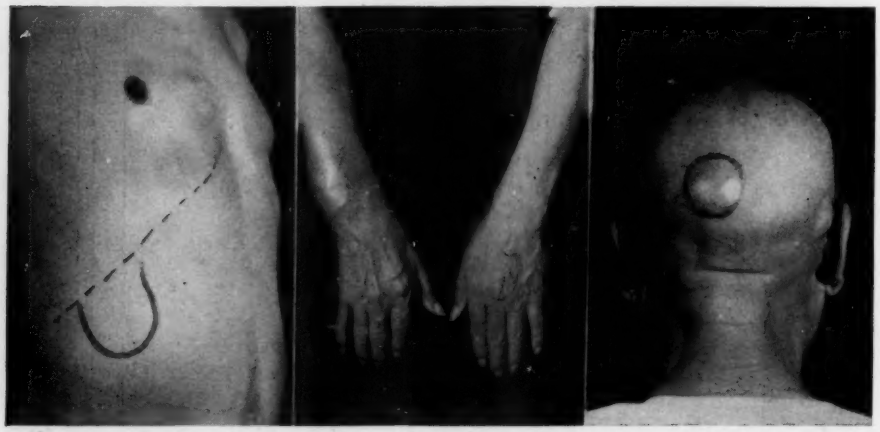

FIG. 1.—Photograph showing the outline of the right kidney extending below the level of the costal margin.
FIG. 2.—Photograph showing the swelling over the distal end of the right forearm.
FIG. 3.—Photograph showing the outline of the swelling over the left occipital region.

swelling, slightly tender and also pulsating, was present in the left occipital region (Fig. 3). Here again, a systolic bruit could be heard. The overlying scalp was normal.

The external genitalia and the prostate gland were essentially normal. The urine was clear and contained no pus cells. The renal function, as estimated by phenolsulphonphthalein excretion, was 60 per cent in two hours. The blood picture showed slight secondary anemia. The figures for the chemical constituents in the blood were within normal limits. The Wassermann reaction of the blood was negative. *Clinical Diagnosis:* Carcinoma of the right kidney with metastases to the skull, the right ulna and the peritoneum.

Cystoscopy revealed the interior of the urinary bladder to be normal. Ureteral catheterization demonstrated obstruction in the right ureter from which urine was not obtained. Bilateral retrograde urograms (Fig. 4) showed a large tumor in the region of the right kidney, the calices and pelvis of which were not filled by the contrast medium.

Excretory urograms (Fig. 5) made following the intravenous injection of 20 cc. of hippuran (12 Gm.) confirmed the previous findings. The right kidney was enlarged, showed calcified shadows in the lower portion, and gave evidence of having lost practically all of its excretory function. The left renal pelvis and calices were fairly normal in appearance and the function of this kidney seemed unimpaired.

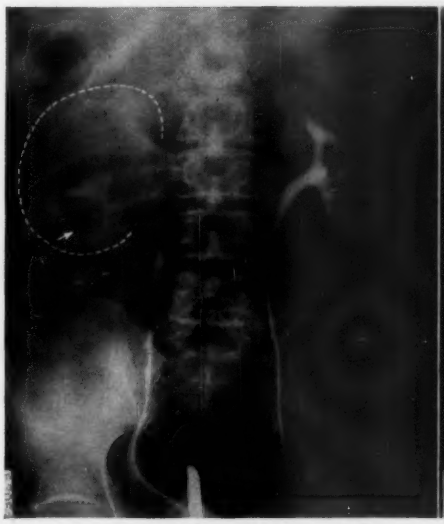

FIG. 4.—Retrograde pyelogram showing a large tumor in the region of the right kidney, the pelvis and calices of which have not been filled by the contrast medium. The arrow points to areas of calcification.

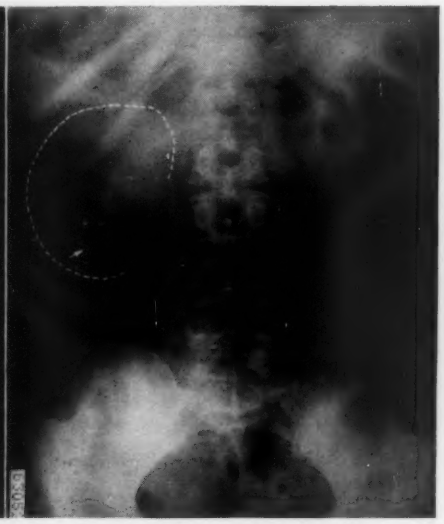

FIG. 5.—Excretory pyelogram which confirms the retrograde pyelographic findings. Note absence of excretion of the dye on the right side.

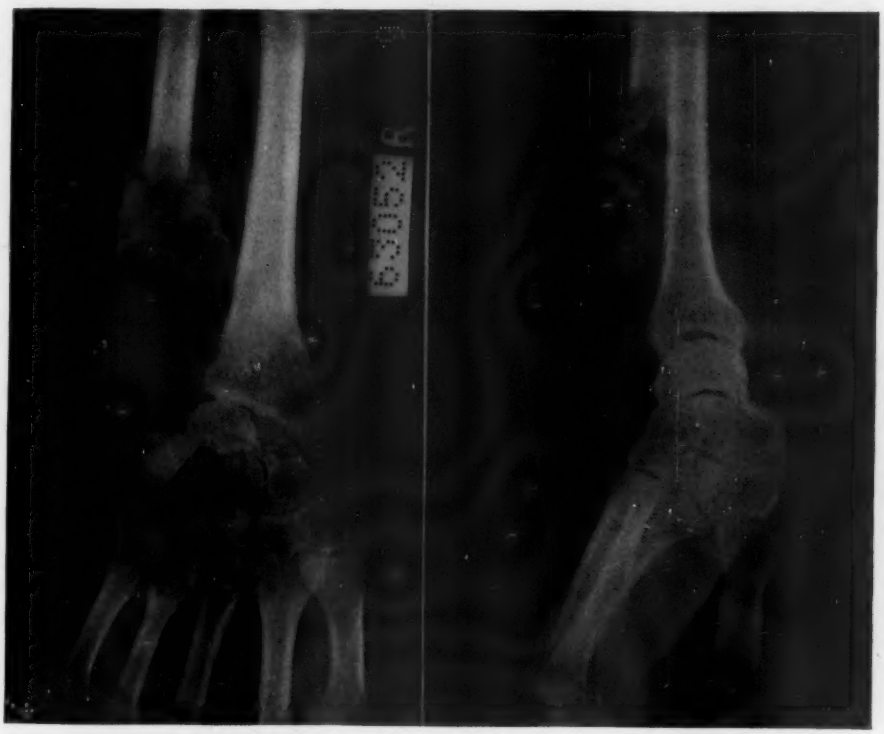

FIG. 6.—Roentgenograms of the right wrist showing destructive lesion of the lower end of the ulna.

Roentgenologic examination further revealed: (1) An irregular erosion, 2.5 cm. in diameter, in the right occipital region, involving both tables of the skull; and (2) destruction and absorption of the distal end of the right ulna (Fig. 6). Careful roentgenologic examination of the chest and the spine revealed no evidence of metastasis to these structures.

A needle biopsy from the tumor of the right ulna was made. *Microscopic Examination* (Fig. 7) revealed epithelial tumor cells which showed a great tendency to form irregular glandular structures separated by a scanty amount of stroma or by capillaries. The tumor cells were cuboidal or columnar with pale and granular cytoplasm which contained a number of small vacuoles. The nuclei were round or oval, generally situated toward the base and contained much chromatin material. Occasional mitotic figures were found. *Histologic Diagnosis:* Adenocarcinoma, which, in view of the clinical and roentgenologic data, was believed to have arisen from the kidney.

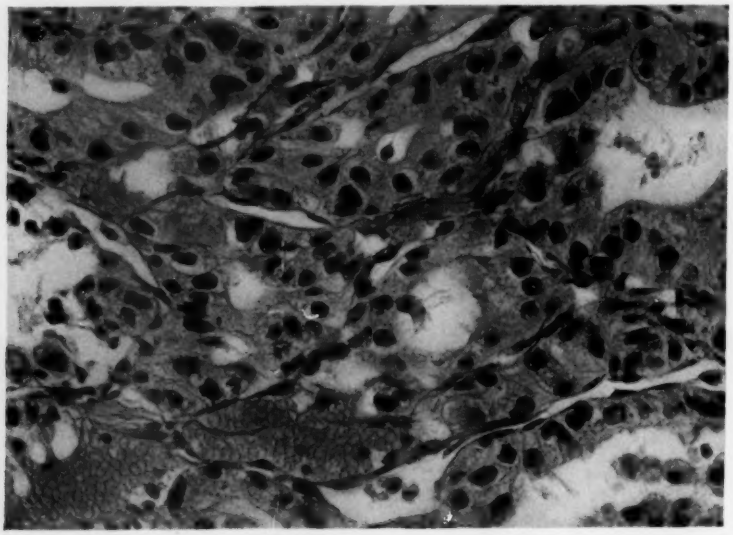

FIG. 7.—Photomicrograph of the metastatic tumor in the right ulna. Note the tendency to form glandular structures. (×295)

On account of his age and the extent of the lesions, the patient refused treatment and returned home where he died four months later.

Clinical Considerations.—This case presents several striking and interesting features. In the first place, it illustrates very well the point that frequently it is the metastatic lesion in the bone which first prompts the patient to seek medical treatment. Diez and Michans[5] state that in 50 per cent of their cases, skeletal metastasis was the first clinical manifestation of an otherwise symptomless hypernephroma. Occasionally the primary tumor may remain silent for a long period, even after a pathologic fracture, due to secondary tumor in bone, has occurred.

Second, the finding in the ulna of a metastatic lesion from any tumor is in itself exceedingly rare. It has been stated[3] that "any bone in the body may be involved but metastases distal to the humerus and femur are infrequent." Risley[6] states that bone metastasis occurs almost entirely proximal to the elbow and knee joints. In an attempt to explain this phenomenon, Piney[7] showed

that metastatic deposits in bone are due to arterial or capillary embolism, that the location of metastases seems to conform to the anatomic distribution of the red marrow and that after puberty the red marrow extends only as far as the upper ends of the humerus and femur. The literature records only 13 instances in which the skeletal metastases from hypernephroma were located distal to the humerus and femur (Table II).

Third, the pulsating character of the metastatic tumor* is noteworthy. Lesions in the bone secondary to hypernephroma are often very vascular, giving a definitely expansile pulsation and audible bruit, so that they may be mistaken for aneurysms. Eschner,[14] MacLeod and Jacobs,[15] Dresser,[3] Cabot,[16] Crile, Jr.,[17] and Roth and Davidson[18] have reported six instances of pulsating tumors of the sternum secondary to a renal hypernephroma, and an aortic aneurysm was suspected in practically every instance. Storath,[19] and Diez and Michans[5] have reported instances of pulsating metastases from hypernephroma to bones of the nose and foot. The latter authors state that 35 per cent of skeletal metastases secondary to hypernephroma show pulsation and give an easily audible systolic bruit. It seems reasonable, therefore, to suggest that any pulsating tumor of the skeletal system should be thoroughly investigated with this possibility in mind, even in the absence of clinical manifestations of a primary renal tumor.

TABLE II

RECORDED INSTANCES IN WHICH SKELETAL METASTASES FROM HYPERNEPHROMA WERE LOCATED DISTAL TO THE HUMERUS AND FEMUR

Author	Location	No. of Cases
de Massary and Weill[8]	Phalanges	1
Garceau[2]	Metacarpals	1
Nitch[9]	Ulna	1
Hand and Broders[10]	Radius	1
Geschickter and Copeland[1]	Tibia	1
Garceau[2]	Tibia	1
Dresser[3]	Tibia	1
von Bergmann[11]	Tibia	1
Pool[12]	Fibula and tibia	1
Geschickter and Copeland[1]	Bones of foot	2
Diez and Michans[5]	Metatarsals	1
Sabolotnow[13]	Tarsals and metatarsals	1
Total		13

Fourth, the roentgenologic interpretation of the lesion in the ulna was not easy in this instance. Baetjer and Waters[20] state that this type of tumor is of medullary origin and that it is impossible to differentiate it from other medullary nonbone producing growths. Gibson and Bloodgood[21] remark that: "As regards the roentgenologic findings, these may be summed up as resembling those of a central sarcoma of the bone. There is never any production of new bone; the cortex may be expanded, there is usually rarefaction of bone in the

* Similar pulsating skeletal metastases have also been recorded in cases of primary carcinoma of thyroid.

neighborhood, and the metastatic shadow tends to be circular in outline. There are no roentgenologic findings which differentiate hypernephroma from any other form of skeletal carcinomatous metastasis." Dresser[3] mentions that in the case of a single metastasis with no signs pointing to kidney involvement, the differentiation between this condition and primary osteogenic sarcoma is practically impossible without the removal of a specimen for microscopic study.

In our present case, the lesion of the right ulna (Fig. 6) showed a centrifugal type of bone destruction, as the shell of the bony growth and the tip of the ulna were still visible. In other words, it was of medullary origin. Its proximal portion was almost cystic in appearance, showing trabeculae and a fairly thick shell which was of wavy outline. The distal portion appeared more osteolytic. The lesion was definitely invasive in character. Periosteal reaction was seen along the shaft just proximal to the growth as well as along the distal end of the right radius. Considered apart from the clinical history of the case, the roentgenographic appearance of the lesion was quite suggestive of primary osteogenic sarcoma or giant cell tumor of malignant type.

SUMMARY

(1) A case of adenocarcinoma of the kidney with multiple pulsating skeletal metastases is reported.

(2) Pulsating tumors in the skeletal system should merit thorough urologic investigation, even in the absence of clinical symptoms of a primary renal tumor.

(3) The distribution and roentgenologic interpretation of the osseous lesions are discussed.

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THE DELAYED CLOSURE OF CONTAMINATED WOUNDS *

A PRELIMINARY REPORT

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THE CLOSURE of wounds is a technical procedure common to most surgical operations. The ideal toward which surgeons have striven is immediate closure of wounds, to be followed by uninterrupted healing. The primary closure of clean wounds is usually successful no matter what methods are employed, but perfection has not yet been reached since infection and dehiscence still occur in a small percentage of wounds thus closed, no matter what technical measures have been employed.

Many studies have been and are being made on the factors that influence wound healing. Suture material, the nutrition of the patient, allergic reactions, air-borne infection, and operative methods have all been shown to play a part in causing the occasional catastrophe to wound healing, and proper observance of the facts brought out by these studies has further diminished the untoward results.

All wounds probably are contaminated to some degree, due to exposure to the air and to the impossibility of sterilizing the skin; yet, due to the remarkable protective power of most tissues, relatively few so-called clean operative wounds become infected. When infection does take place, it is generally assumed that there has been an error in technic or that an unusual relationship exists between the bacteria and the tissue.

Not infrequently, an otherwise clean wound may become contaminated during the course of the operation because of conditions met in the tissues at the site of the operation. If frank sepsis is encountered and drainage is indicated, the wound will necessarily become infected along the course of the drain. Occasionally a focus of infection such as the interior of the colon may be encountered during operation, in which case drainage is not indicated, and although it is desirable that the wound in the abdominal wall heal without interruption, infection may develop in it to the detriment of the patient. The handling of wounds thus contaminated is still capable of improvement. A method we have used in handling such wounds recently has been helpful to us and will be described.

Infected wounds have always occurred in the human race. The susceptibility of vertebrates to infection increases as one passes up the evolutionary

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scale. This diminution of resistance to infection in the higher vertebrates is paralleled by a progressive loss of the ability to repair tissue damage as compared with the remarkable ability in the lower forms of animal life to regenerate whole limbs and organs.[1]

The closure of frankly contaminated wounds such as those associated with open approaches to the gastro-intestinal tract, especially in its lower portions, such as colostomies, cecostomies, and inadvertent openings into the colon and rectum, has never been entirely satisfactory. Although many successful primary closures of such contaminated wounds have been carried out, the incidence of infection in them has always been high, carrying with it a prolonged convalescence and a higher mortality. Examination of our own records showed about a 50 per cent occurrence of serious wound infection in the wounds contaminated through some contact with the interior of the lower gastro-intestinal tract.

It has been customary in such cases to place a drain in the wound to provide a route of exit for the exudate of infection to pass when contamination passed to infection. Occasionally the drain, thus placed, was effective; more often the infection became so extensive as to necessitate the removal of all sutures and eventually necessitate secondary closure when the infection had abated.

In 1917, the French surgeons[2] developed a method of treating potentially contaminated war wounds, called delayed primary closure. It was applied to all wounds in soft tissue, 15 hours or more old, except those of the scalp, face and hands. The method consisted of the usual careful cleansing of skin and deeper aspects of the wounds; wide débridement; culture of the wound; constant flooding of the wound with Dakin's solution or other antiseptic; and wide packing of the wound with flavine gauze. The patient was then sent to the Base Hospital, marked for delayed primary closure. Within 24 to 48 hours, the bacterial flora of the wound was known, and if streptococci were not present, and if there were less than five colonies per plate, the pack was removed and the wound closed under anesthesia. The method had many advantages in that the Field Hospitals and Dressing Stations were emptied rapidly. The first cultures were available early and infections by the streptococci, which carried the highest morbidity and mortality, could be sorted out and treated more adequately. Finally, the surgeon who closed the wound was able to follow it personally. Fraser,[3] in 1918, reported an incidence of 9.7 per cent failure in 41 cases of primary closure as compared with 4.5 per cent failure in 63 cases of delayed primary closure. He also reported 31 bacteriologically negative wounds from 35 contaminated wounds after 48 hours' treatment by delayed primary closure, employing a flavine pack in the wound. In 1918, delayed primary closure of all soft-tissue wounds, excepting those in the scalp, face and hands, was advised by the surgeons of the American Expeditionary Force.[4] The best results were obtained when the wounds were closed within 50 hours.

The differentiation between delayed primary closure and secondary closure is usually interpreted as one of tissue repair rather than that of time. Pool[5] defines delayed primary closure as the approximation of wound edges without excision, while secondary suture is taken to mean that the epidermis has grown inward over the granulations and must be excised and lifted before good approximation and union can be obtained. In late secondary closure, granulation tissue must also be excised.

During the past few months, a method of delayed closure of frankly contaminated wounds has been carried out that has given fewer infections and a much higher incidence of uninterrupted healing than was secured by the primary closure of such wounds with or without drainage. Its employment has been largely confined to wounds contaminated during operation upon the lower bowel. The method is not in any sense unique, since surgeons have, from time immemorial, packed wounds with various substances with the expectance of closing them later, and it has been a common practice to pack wounds contaminated during appendicectomy without even applying sutures.

This method was first employed by us on a patient with a carcinoma of the sigmoid colon. Previous to his entrance to the University Hospital, he had developed acute intestinal obstruction and an operation had been performed to relieve this obstruction. The cecum had been delivered through a right rectus incision and he still presented most of the cecum in this wound when first seen by us. The original incision was badly placed for resection of the lesion in the sigmoid, so an incision was made through the left rectus muscle and the lesion resected and an end-to-end anastomosis made. There was, unfortunately, some contamination of the field during this procedure. The peritoneum was closed with double No. 000 plain catgut and the fascia closed with interrupted sutures of a No. 30 stainless steel wire. It was certain that the wound was contaminated both from proximity to the cecostomy and because of misfortune during the anastomosis. It was decided to pack the subcutaneous tissue with flavine gauze, but to place fine silk sutures to be tied later since it seemed inevitable that infection would occur. Cultures were taken which showed the usual intestinal flora. The next day the pack was removed, cultures again taken, a biopsy secured from the wound and the sutures tied, thus securing approximation of the wound. The wound healed without event. Later the cecum was closed, returned to the abdomen, and the wound associated with this approximated in a similar manner, again with a good result.

Since then we have employed this method of wound closure, under similar circumstances, upon 21 patients, the details of which are shown in Table I. As can be seen, we have secured uninterrupted healing without infection in all except one instance, in which a small abscess containing about 1 cc. of pus appeared in the wound; this cleared up rapidly following evacuation of the exudate.

In all cases, the wound has been closed as described, namely, with con-

TABLE I

TWENTY-ONE CASES OF DELAYED CLOSURE OF CONTAMINATED WOUNDS

No.	Name	Diagnosis	Operation	Healing
1	A. T.	P.O. carcinoma of sigmoid	Closure of colostomy	No infection
2	J. M.	P.O. carcinoma of sigmoid	Closure of cecostomy	No infection
3	J. M.	Carcinoma of sigmoid	Obstructive resection	No infection
4	A. L.	Carcinoma of sigmoid	Obstructive resection	No infection
5	A. L.	P.O. carcinoma of sigmoid	Closure of colostomy	No infection
6	E. H.	Carcinoma of sigmoid	Obstructive resection	No infection
7	A. H.	Perf. diverticulum	Obstructive resection	Minor infection
8	A. H.	P.O. diverticulum	Closure of colostomy	No infection
9	R. C.	P.O. carcinoma of rectum	Revision of colostomy	No infection
10	A. M.	P.O. carcinoma of rectum	Bilateral herniorrhaphy	No infection
11	L. W.	Ulcerative colitis	Right colectomy	No infection
12	B. W.	P.O. regional ileitis	Closure of colostomy	No infection
13	E. K.	Fecal incontinence	Closure of colostomy	No infection
14	W. K.	Perforated appendix	Appendicectomy	No infection
15	L. L.	Regional ileitis	Exclusion of ileum	No infection
16	W. G.	Biliary fistula	Closure of fistula	No infection
17	I. D.	Fecal fistula	Closure of fistula	No infection
18	M. M.	Ulcerative colitis	Left colectomy	No infection
19	T. G.	Carcinoma of rectum with perforation	Combined abdominoperineal resection	No infection
20	J. S.	P.O. perforated appendix	Excision sinus	No infection
21	M. H.	P.O. carcinoma splenic flex.	Closure of colostomy	No infection

tinuous sutures of fine catgut in the peritoneum and interrupted sutures of stainless steel wire in the fascia. Various ways of applying the silk sutures to the skin and subcutaneous tissue have been tried but the near-far, figure-of-eight method has been found to be the most satisfactory. The flavine pack need be only large enough to cover the denuded areas and is best applied in two portions, one from each end, to meet in the middle, because they are removed more easily than one long pack. The method is shown in Figures 1 and 2.

The patients complain of very little discomfort at the time of the removal of the pack and the approximation of the wound when tying the sutures. When the pack is removed, it has been a uniform observation that the wounds appear dry and there is a certain stickiness to the surfaces that aids the closure. Microscopic study of sections of the wound edges, at 24 hours, shows an exudate which consists of fibrin, in the meshes of which are polymorphonuclear leukocytes, wandering cells, some necrotic tissue and many young fibroblasts. Several wounds have been left for 48 hours before removal of the pack, and sections of the wound at this time show more fibrin, many more leukocytes and a definite increase in the number of fibroblasts. The characteristic reaction seen in the margins of the wound is shown in the photomicrographs in Figures 3 and 4.

Howes, Sooy and Harvey[6] have described a "lag-period" in wound healing, during which time the wound has little if any tensile strength. This period lasts from four to five days and corresponds to the stage of exudative reaction

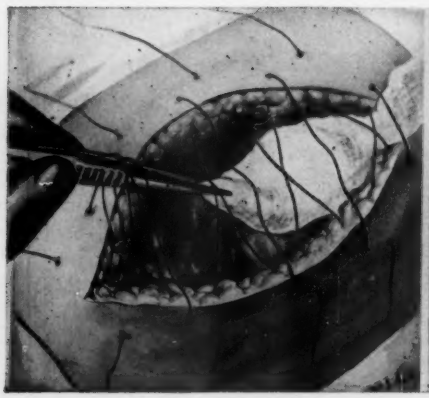


FIG. 1.—Acriflavine pack being placed in wound.

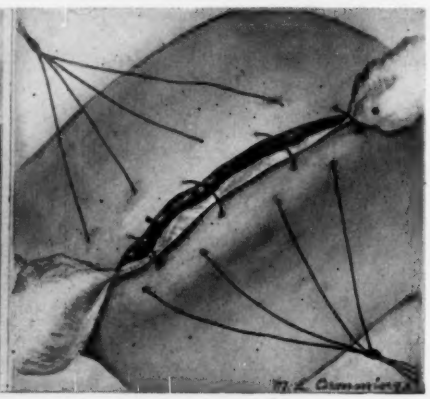
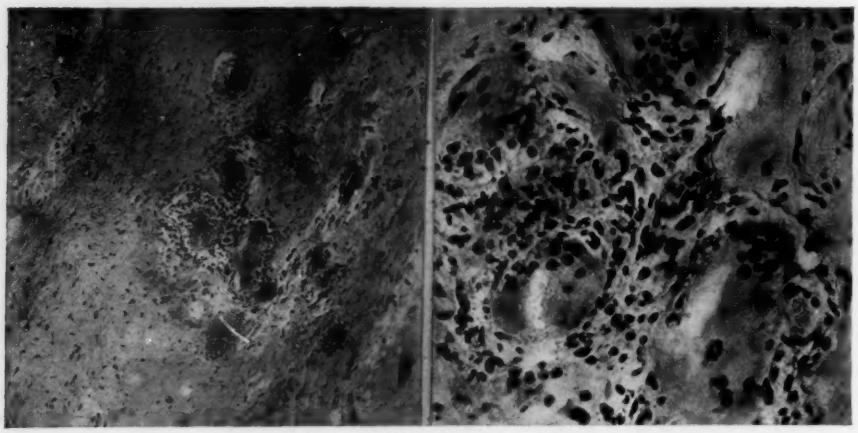
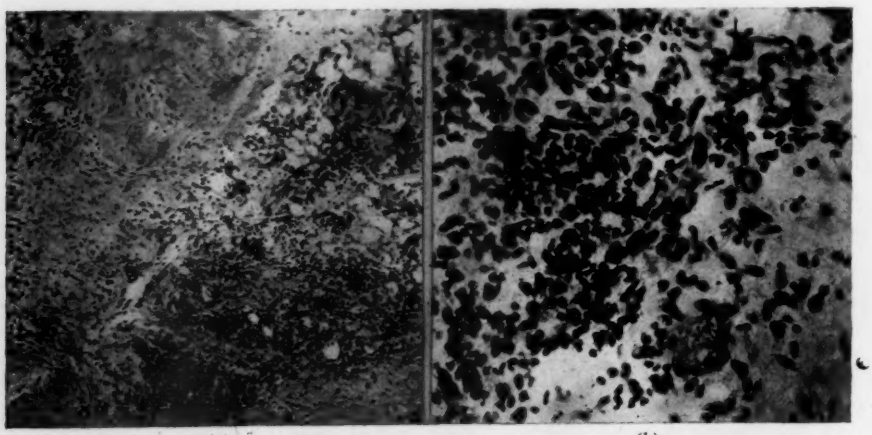


FIG. 2.—Acriflavine pack in place.



(a) (b)

FIG. 3.—(a): Biopsy of wound 24 hrs. p. o. at time of delayed closure. (×185) (b) Same as above. (×750)



(a) (b)

FIG. 4.—(a): Biopsy of wound surface 48 hrs. p. o. at time of delayed closure. (×185) (b) Same as above. (×750)

in wound healing. The critical time for the wound, as far as infection is concerned must occur during the exudative reaction before fibroplasia begins. DuMortier[7] smeared *Staphylococcus aureus haemolyticus* over the suture line of guinea-pig wounds at various time intervals postoperatively, and found that, up to six hours, postoperatively, the wounds were infected in 100 per cent of the cases with many virulent widespread infections of the entire abdominal wall. Twenty-four hours postoperatively, 66 per cent of the wounds were infected; 48 hours postoperatively, 56 per cent infections; four days postoperatively, 10 per cent infections; six days postoperatively, no wound infections; after six hours postoperatively, all wound infections were local and without systemic reactions. It has been suggested that after coagulation of the fibrin occurs, the resistance of the wound is greatly increased because of the accompanying sealing off of the capillary and lymph spaces, tending to keep infection localized or below the clinical horizon. Delayed closure of contaminated wounds, such as described, must, in a similar way, carry the wound through this critical period, probably by aiding coagulation of the fibrin so that when the wound surfaces are brought together a more unfavorable environment is present for the bacteria in the wound.

No additional benefit has been noticed from leaving the pack in the wound for two days; and at present we are removing the pack and tying the sutures 24 hours after operation. Cultures have been taken from the wound at the termination of the operation in ten cases, all of which showed dominantly *B. coli* with fewer *Staphylococcus aureus* and *Streptococcus anhaemolyticus*. Cultures were also taken on the same wounds at the expiration of 24 hours, and these were still positive with the same bacterial characteristics. Consequently, the packing of the wound apparently has no bactericidal effect, although we cannot state that it may not have a bacteriostatic one.

Since the peritoneum and the fascia have been contaminated to the same degree as the skin and subcutaneous tissue and these layers have not shown infection in spite of being closed by sutures, one might assume that they have a higher degree of resistance to infection than has the subcutaneous tissue. This observation and clinical experience suggest that infection in wounds of the abdominal wall frequently begin in the subcutaneous tissue and spread to deeper layers from this plane. The low resistance of fat to infection is well known. It is known that from eight to twelve hours usually elapse before infection supervenes in a contaminated wound, and it is possible that the irritation of the gauze produces an early inflammatory reaction in the subcutaneous tissue that is protective and that inhibits the transition from contamination to infection.

Experimental work to determine this point is under way. We have neither tried the administration of sulfanilamide to these patients, although it may well be useful in those wounds contaminated by the *Streptococcus haemolyticus*, nor have we tried the local use of antiseptics, including washing with soap and water, as suggested by Jackson;[8] therefore, we cannot contrast these

methods with the one described. It is obvious that contamination by certain virulent organisms, or by the common organisms, in patients with lowered resistance may give rise to serious infections if contamination occurs. Judging from this limited experience, we believe that delayed closure of wounds of the abdominal wall may be helpful in the occasional case where contamination has occurred either because of the nature of the surgical problem or because of accidents in technic.

SUMMARY

A method of delayed closure of contaminated wounds has been described with a report of 21 consecutive successful wound closures without serious infection.

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DISCUSSION.—DR. DERYL HART (Durham, N. C.): I will restrict my discussion to the paper of Doctor Walters. First, I want to emphasize that we do not consider contaminated air as the only source of wound infections. It assumes a position of major importance only after other sources such as supplies, instruments, and skin have been eliminated or reduced to the minimum. In our own operating rooms we believe that the air contaminated with pathogenic bacteria given off from the respiratory passages of human beings was the greatest source of danger to the open wound until steps were taken to remedy this condition. Since this hazard has to a large extent been removed, we have had a most striking improvement in our results, as indicated not only by reducing the infection rate in clean primary incisions from 4 per cent to less than 1 per cent, but there has been no serious infection in such wounds, and the patients whose wounds did not show signs of suppuration have had much less local and systemic reaction. The postoperative temperature elevations have been lower and of shorter duration.

There are wide variations in the number and type of organisms found in the air, corresponding to similar changes in the nose and throat flora of the occupants of a given area. We rarely have many carriers of the hemolytic streptococcus, but the respiratory tract carriers of the *Staphylococcus aureus* have varied from 15 to 80 per cent of the general population. On the basis of cultures of the air made in other operating rooms over the country we feel that this distribution of staphylococci must be widespread. Our wound infections were caused almost entirely by the hemolytic yellow staphylococcus, a streptococcal operating room infection being almost unknown. This

might be contrasted with the report of Walker from a teaching hospital in Boston where, during an epidemic of streptococcal sore throats, approximately 10 per cent of their operative wounds became infected with the hemolytic streptococcus.

During the first six years of the Duke Hospital, before instituting bactericidal radiation in the operating rooms there was a total of 15,557 operations. During this time there were at least seven deaths from infections in clean incisions on the general and neurosurgical services alone: three extrapleural thoracoplasties, primary stage; one extrapleural thoracoplasty, secondary stage; two craniotomies; and one radical mastectomy, all caused by the hemolytic *Staphylococcus aureus*. During the next three years, 10½ months, or up to December 1, 1939, out of a total of 23,213 operations, 1,062 clean, primary operations and 105 clean secondary operations (reopened wounds), on the general, orthopedic, and neurologic surgical services, were performed in a field of bactericidal radiation. Even though most of the larger operative procedures such as thoracoplasties, arthroplasties, bone grafts, laminectomies, craniotomies, ventral herniorrhaphies, *etc.*, were included in these groups, not one of these patients died as a result of, or had his life seriously threatened by, an infection in the wound. During this same period one patient having a craniotomy and decompression performed for an inoperable left cerebral glioma, when bactericidal radiation was not available, died of meningitis caused by the hemolytic *Staphylococcus aureus*.

During the 12 months from November 1, 1938, to November 1, 1939, there were over 600 clean, primary incisions made in a field of bactericidal radiation with only one postoperative wound infection of sufficient note to be diagnosed at the time of the patient's discharge from the hospital. This occurred in a patient having a laminectomy immediately following injury, the operation being performed through skin which showed superficial abrasions, and deeper tissues which were contused and infiltrated with blood. In spite of such a condition of the skin, this infection was thought to be hematogenous since it came on nine days after the operation, and five days after a postoperative pneumonia with an associated septicemia, pyelitis, and cystitis, all caused by the hemolytic *Staphylococcus aureus*. On careful review of each of these records there were five other mild, or questionable, wound infections as follows:

(1) Herniorrhaphy—stitch abscess. Maximum temperature 99.5° F.
(2) Craniotomy—stitch abscess.
(3) Open reduction old fracture dislocation of ankle, lengthening tendon of Achilles. Skin necrosis. Infection limited to denuded and exposed area; joint not involved.
(4) Arthroplasty hip—vitallium cup inserted; and superficial drains—postoperative hemorrhage. Infection limited to drainage tract, joint not involved—apparently retrograde infection from skin.
(5) Thoracoplasty; extrapleural—hematoma in incision; drained. Considered not infected by those who dressed it, but a positive growth of *Staphylococcus aureus* was obtained from the draining blood clot. Second stage performed 29 days after first stage.

We feel that by greatly reducing the number of viable pathogenic bacteria in the air about the wound and sterile supplies, we have reduced our postoperative wound infections by over 75 per cent and greatly diminished their severity, at the same time improving wound healing following most of our larger operations.

In regard to the work of Devenish and Miles, it is my opinion that they were dealing with a special condition. Cultures of the skin of one surgeon consistently showed a heavier contamination with a more pathogenic strain of yellow staphylococci than similar cultures taken from the skin of another surgeon and other members of the operating teams. With many punctured gloves, naturally, the surgeon with the more highly contaminated skin had the greater percentage of infected wounds since the hands cannot be completely freed of organisms. When the skin of a patient or his surgeon is known to harbor more virulent yellow staphylococci as indicated by recurring boils, operations of election should be postponed until such a condition can be eliminated.

Whether or not one considers the air to be an important medium for transporting pathogenic bacteria to operative wounds and whether or not one undertakes to remedy the condition, one must not neglect other sources of contamination and must maintain a surgical technic which leaves his wounds in the best condition for the body defenses to handle the bacteria which gain access. Regardless of how aseptic conscious we may be and what measures we may employ, we have not yet attained such ideal conditions that we can operate with assurance that no pathogenic organisms will reach the wound. Fortunately the wound that is in the best condition to handle the bacterial contaminants is also in the most ideal condition for healing.

Dr. Roy D. McClure (Detroit, Mich.): I would like to ask Doctor Coller whether or not he made anaerobic cultures in these wounds. Dr. W. A. Altemeier,* of our staff, has been taking both aerobic and anaerobic cultures from cases of peritonitis and wound infection secondary to appendicitis or intestinal surgery. Mixed cultures containing as many as five to seven different species of bacteria were usually obtained by him. The anaerobic organism frequently predominated. He has found the virulence of these bacteria in pure culture to be very low for laboratory animals. Collectively, however, three or more strains have a high degree of synergitic pathogenic action, producing large areas of cellulitis and gangrene when injected subcutaneously.

The treatment of such wounds with zinc peroxide, as advocated by Meleney, has been very successful in our hands, when combined with adequate drainage. Perhaps part of Doctor Coller's success was due to the inhibitory effect of the air upon growth of anaerobic organisms.

Dr. Hugh A. Gamble (Greenville, Miss.): I have been interested in the work of Miles and Meleney ever since their early reports. Their work certainly merits most careful consideration.

There is one feature in regard to infection of wounds which has not been brought out in the discussion this morning, and that is the prominent part played by droplet infection from talking over wounds during an operation.

Some two years ago, a Vienna surgeon reported a series of 1,000 clean operations without a single infection. He laid stress upon the fact that he felt that most infections of clean wounds were due to inadequate masking and unnecessary conversation over the patient. He instituted, in addition to thorough masking, a non-talking technic applicable to everyone in the operating room, using sign language only, and allowing no conversation. To this change he gave full credit for his excellent results.

Shortly after reading this article we instituted a similar regimen in our services. In the period of time since then, my brother and I have performed

* Altemeier, W. A.: The Bacterial Flora of Acute Perforated Appendicitis with Peritonitis: A Bacteriologic Study Based upon 100 Cases. Annals of Surgery, 107, 517–528. April, 1938.

approximately 3,000 clean operations and have had three wound infections in that number. We are convinced that elimination of talking has played a major rôle in the reduction of infections of this character. It is a technic easily learned and consists simply of the use of sign language for instruments, sponges, linen, *etc.*

Referring to Doctor Coller's paper upon the method of treatment of wounds, we have advocated a similar procedure both in season and out of season during the last 16 years. First, in 1924, I read a paper before the Mississippi State Medical Association advocating the leaving open of such wounds and also those more virulently infected than the ones Doctor Coller has shown. In potentially infected abdominal wounds, particularly those associated with peritonitis, intra-abdominal abscesses, intestinal obstruction, gangrenous appendices, you are sure to have infections, principally with anaerobic organisms. In the closed wound these infections find an ideal incubator and culture medium and spread in the fascial planes and between the skin and fascia with, at times, most astonishing rapidity and catastrophic results.

Before adopting the open treatment of the potentially infected wound I have seen a number of infections of this character, and reported before the Southern Surgical Association 12 cases of fulminating gangrene of the abdominal wall occurring in the closed or partially closed, potentially infected wounds. Leaving the wound open allows air, which is a specific for this type of infection, to reach all portions of it, and provides for free drainage. Since adopting this plan of treatment for the potentially infected wound, we have had no cases of spreading infection of the abdominal wall.

In the type of case which Doctor Coller reports we feel that he is right in closing it secondarily, but in the type of wound acutely infected with virulent anaerobic organisms, closing the wound after removing the pack is inviting trouble.

As to the manner in which the pack acts in its effect upon the wound it is our opinion that it has: (1) A bactericidal effect; (2) it causes a reversal of the flow of lymph; and (3) it limits the spread of infection by the formation of a barrier of inflammatory tissue.

We are definitely of the opinion that the mortality rate in acute intra-abdominal catastrophes such as ruptured appendices, gangrenous cholecystitis, suppurative peritonitis and intestinal obstruction, *etc.*, is more often due to anaerobic infection of the soft tissues of the abdominal wall and complicating sequelae than to any intra-abdominal pathology. Since adopting the open treatment of abdominal wounds in such lesions, our mortality rate has been lowered to such an extent that we have largely lost the dread of these conditions.

In a recent review of the cases of generalized diffuse peritonitis secondary to appendicitis, 158 in number, treated, since 1924, by leaving the wounds open, our mortality rate has been under 2 per cent.

DR. FRANK K. BOLAND (Atlanta, Ga.): I would like to ask Doctor Elkin whether he has ever made cultures of the catgut used in hospitals. We sterilize everything else, but accept catgut as being sterile. Did he ever estimate the difference in cost between silk and catgut? Silk is much cheaper, which is an important item, especially in a large city hospital.

DR. FREDERIC W. BANCROFT (New York, N. Y.): I think there is another source of contamination of wounds that has not been mentioned. Dr. Kingsley Roberts, on my staff, a number of years ago took cultures of the

peritoneal cavity in presumably clean cases. He would take the peritoneal strip up very gently, cauterize it and put in a small applicator and take a culture. These were presumably clean wounds, but he had a 72 per cent culture growth. It is my impression that nothing is sterile. It is true that 60 per cent of these were nonpathogenic organisms. We must, therefore, consider that contamination may be present, and use gentleness and care as well as all the protective measures we know. These were cases of noninfected, clean celiotomies, such as hysterectomies for fibroids, chronic appendices, *etc.*

Dr. Wm. H. Prioleau (Charleston, S. C.): I would like to cite briefly my experience with suture material in thyroid operations. For some years I used fine, plain catgut. In a majority of the cases there was a discharge of serum from the wound. Because of this objectionable feature I changed to the use of fine, black silk. With it the healing was far superior, there being much less induration, and only, occasionally, the drainage of serum. However, in one instance of a severe wound infection, there resulted the extrusion of silk knots over a period of months. This forcibly brought to my attention that the satisfactory use of silk was based upon certain conditions over which I did not have absolute control—such as the operating room technic of rotating internes, some with no previous experience, and student nurses being coached by supervising nurses during the progress of the operation. I next tried fine (No. 00–000) chromic catgut, which I have been using with satisfaction for several years. It fills a midposition between silk and plain catgut. There is a moderate amount of wound induration, but only seldom the discharge of serum. In one case there was the extrusion of a few knots. In case of infection, it gives no particular trouble. It is to be avoided subcutaneously as it sometimes forms small nodules, or sterile abscesses.

I have found great satisfaction in the use of fine alloy steel wire in the repair of herniae, and the closure of celiotomy incisions, particularly in the presence of infection. In the presence of wound infection, it is preferable to silk in that the wire does not become extruded, nor does it act as a focus for sinus formation.

Dr. W. A. Bryan (Nashville, Tenn.): It seems that everybody here agrees that we cannot get rid of bacteria. I think everybody understands that. All we can do is reduce them to as safe a minimum as possible. Doctor Elkins, I think, said that the resident who had 82 cases in the hospital at Atlanta must have done something. I am wondering if his result did not come because he did not do something. That is what I would like to talk about. You know that dead tissue is a much better culture medium than live tissue. We know that traumatized tissue is a much better culture medium than nontraumatized tissue, and we know that tissue in which there is poor circulation or no circulation, although it is still alive, is a better culture medium than where the blood is still circulating. Everybody knows that. Wounds of the face get well readily; wounds of the feet and various other parts of the body do not. Some of us were brought up in the country and when we had to tie a pig we tied him tight so that he would not get loose; you had to tie a bag of oats so that it would not leak. Now we brought that idea into the surgical field and in our overanxiety that the wound should hold we tied the sutures in it good and tight, tight enough to constrict the tissues, and still a little afraid, we tied it still tighter and killed the tissues. This offers a field in which bacteria can grow if they get in.

As between catgut and silk I use one sometimes and sometimes the other. I do not know how much difference there is. I do believe there is a differ-

ence between large ligatures and small ones, and also in masses of material introduced into the tissues. If your assistant gets a wad of fat, or tissue, or ligament inside the forceps and you tie it tight enough it leaves a good site for the culture to grow within the wound. I wonder if one of the differences in favor of silk as opposed to catgut is not the fact that silk will not stand the pull. When you tie with silk you cannot bring it too tightly together because it will break. And, in addition to all that has been done toward reducing the number of bacteria so far as possible and doing whatever you please, I think one of the keynotes is handling of the patient's tissues gently and causing as little trauma as possible. Sutures should approximate tissues, not constrict them.

DR. CHARLES C. GREEN (Houston, Tex.): I have a very definite opinion about silk and catgut. " 'Everyone to his own liking,' said the old lady when she kissed the cow." I have lived long enough to see this thing come up and go away and come up again. We have heard the older surgeons tell of the advantages of silk over catgut, then have heard them reverse themselves. You could not make Alton Ochsner use anything but silk, but he has not lived long enough to see it come and go. I think the most convincing argument is to check our own results. I took 100 cases and used silk, and a second 100 cases and used chromic catgut, and in my hands catgut was far superior to silk. You know they tell you: "Oh, yes, you do get a sinus or a fistula sometimes." But they do not tell you they last for three or five or six months—that is passed over quickly. I do not think you can deny the fact that the longer a foreign body stays in the tissues the more trouble it causes. Catgut is absorbed much more quickly than silk, consequently it is much less likely to cause infection, with sinus formation, than does silk.

DR. RUDOLPH MATAS (New Orleans): I fear that what I am about to say will sound like a very discordant note in this discussion. It is the result of a recent experience in the Military Hospitals of Catalonia during the later months of the so-called Republican régime in Spain. I am referring to the method of treating compound war fractures of the extremities which abounded in all the surgical services and in fact had one entire hospital exclusively devoted to their care. I remained in the Catalonian war zone for over two months while being delayed in the securing of passports for relatives whom I wanted transferred to safety in France.

As a nonpartisan American surgeon, concerned essentially in the medical aspects of the war, speaking the language fluently, with many old friends in the medical profession of the country, I was treated with every courtesy and given free access to all the hospitals and medical centers in the war zone.

I saw many practices, especially in the treatment of war fractures, which, in the light of the present discussion on the importance of atmospheric contamination, were amazing as surgical heresies.

I must say that whatever preconceived notions I had of the treatment of war wounds—derived chiefly from the experience of the World War—were completely upset by what I saw in the Catalonian war zone. The military and civilian hospitals in Barcelona alone, where over 5,000 wounded were under treatment; in Gerona, likewise, crowded with wounded who were being rushed in carloads from the battle front on the Ebro and the Segre, provided an inexhaustible clinic for the study of the most varied war wounds.

The patients were all young men, the flower of the youth of the country—battered, crushed or crippled from the effects of rifle, machine gun, shrapnel, shell and aerial bomb explosions—a fearfully tragic sight to contemplate.

My most interesting experience was at Banolas, near Gerona, where an old monastery had been transformed into a base hospital exclusively devoted to war fractures—except those of the skull with brain injury, which were referred to Neurosurgical Services in other hospitals. I never imagined that one could see such an aggregation of fractures as I saw assembled at Banolas. There were great halls in which several hundred fractured men were treated in separate divisions, classified according to the anatomic seat of the fracture. In one ward devoted exclusively to fractured *femurs*, there were 75 or more patients under treatment; as many, or more, in other divisions for fractured legs; and even more numerous in wards for fractured shoulders, arms and forearms. What an incomparable but lost opportunity for the education and training of a school of young surgeons was the thought that frequently recurred in the presence of this immense mass of traumatized bones and joints!

The fractures of the *femur*, all compound (there were no "simple" fractures in warfare), often multiple, and comminuted, with great lacerations of the soft parts, commanded special attention; not only because of their gravity, but as tests of the efficiency of the revolutionary methods of treatment adopted in the Catalonian hospitals in which antiseptics were totally discarded. The Carrel-Dakin treatment had been tried unsuccessfully and abandoned early in the war. With the great crowding of wounded and inadequate trained help, the rigorous application of the method had proven ineffective, especially since the simplified technic based on the procedures of Winnett Orr (of Lincoln, Nebraska) and Lorenz Böhler, of Vienna, enormously simplified the care of the wounded and yielded better results. The only relic of the World War that remained in the practice of this war was *débridement*, which was the initial procedure in all cases, after hemorrhage and shock had been attended to in the casualty stations and field hospitals. The greatest stress was laid upon the excision of all dead, dying or doubtful tissue and the reduction and setting of the fractures under the fluoroscope or by radiographic control, while the limb was kept in complete extension on a suitable fracture table (Putti's, Böhler's, *etc.*) While in full extension, under general or spinal anesthesia, the wound was packed with plain sterile gauze so as to reach and drain every recess or pocket where the wound secretions could accumulate. With the fracture set, the wound packed and the limb in full extension, a plaster encasement was applied in hand-molded gauze-plaster sections (not roller bandage) directly in contact with the skin and the wound without any interposed stockinet or padding of any sort, in order to prevent any possible motion under the plaster. The limb, thus thoroughly encased in a close fitting spica, extended from the foot to the waist, including the pelvic girdle. By this procedure, the plaster received the discharges from the wound directly, and soon became soaked with them, but the plaster dried and was not removed for three or more weeks, unless there was evidence of abscess or spreading infection, or gas gangrene, an extremely rare event. After the second week the patients were encouraged to move out of bed with the help of a walking stick. The number of patients with fractured thighs who were seen walking about the grounds in their full-length plaster spicas, with only the help of a walking stick—all seemingly lively and happy—is one of the strange sights that greeted me on entering the hospital grounds.

There seemed to be universal agreement on *débridement*, reduction under mechanical traction and anesthesia, controlled by radiograms or the fluoroscope, with packing of the wound, free drainage into a completely closed and immobilizing plaster encasement, which was allowed to remain, *in situ without change*, until the healing of the wound had advanced sufficiently to become protected by granulation, against secondary infections.

While the fundamental principles of the fracture treatment were the same in all the Catalonian hospitals, there were differences in the methods of reducing and setting them.

Dr. F. Jiméno, the chief at Banolas, a most devoted pupil of Böhler, of Vienna, and thoroughly trained in his methods, resorted to skeletal traction with Kirschner's wire and stirrup tractors, Schmerz's tongs and Steinman's pins—in fact, his wards could have passed easily for a German military clinic except for the patients, who spoke Spanish. As a rule, he resorted to gradual reduction by skeletal traction before packing and encasing the limb in plaster.

Dr. Joseph Trueta, chief of the State Military Hospital, in Barcelona, avoided skeletal traction and depended, for reduction, on mechanical extension, availing himself of the open wound and débridement to secure the most perfect apposition of the fragments. After packing, the immobilization of the limb followed with the plaster encasement applied during extension. At first, the wound was packed with vaselined strips of gauze as applied by Orr, but the vaseline gave out and the sterile gauze, alone, was used. There were few cases in which primary suture of the wound had been attempted. All wounds, with few exceptions, that were brought in ten or more hours after the injury were enclosed in the plaster encasement without suture, secondary sutures being applied after the wound had become healthy and filled with granulations.

I had an opportunity to see several plaster encasements removed from arms and thighs after they had been *in situ* for from 15 to 21 days. The stench of the soiled encasement was nauseating. A magma or mush of decomposing pus, wound secretions, including sweat and other matter, covered the surface of the wound under the plaster bandage. But after wiping this off with warm water and soap, and when the packs were removed, I was surprised to see the excellent, healthy, pink, well-granulated appearance of the wounds, coupled with a very satisfactory condition of the patients—no fever, no pain, good appetite, *etc.* This was indeed a revelation which I had not anticipated. Why, no acute streptoccocal infections, little or no tetanus, gas gangrene, *etc.*, was indeed an extraordinary fact which many theories attempt to explain, but are too long to occupy our attention now. Suffice it to say that when fresh wounds are relieved of all dead or devitalized tissues, they are, when put to complete rest, quite able to take care of themselves without the aid of antiseptics, which (when truly bactericidal) hinder the normal reproduction of the tissue cells and weaken their defenses. At any rate it would seem that a symbiotic existence is possible between the normal tissue cells and the saprophytic bacteria and other pathogenic organisms that gather under cover of a plaster encasement. In fact, if there was one essential for the successful treatment of fractures, it was plaster of paris. By the close of the war, plaster had risen to the level of an apotheosis in surgical esteem.

While in Banolas, Doctor Jiméno kindly gave me a statistical summary of his experience in 6,000 fractures which had been treated under his direction since the beginning of the war, of which 500 were fractures of the femur, which had been treated with a total mortality of 16, or 3.2 per cent! There were five amputations—four necessitated by septic infection, and one by gas gangrene which had appeared before admission to the hospital.

Doctor Trueta,* in his little monograph on the treatment of war wounds, was the first to formulate the Catalonian method on the basis of Winnett Orr's teachings, which he practiced early in the war with most satisfactory results.

* Joseph Trueta, M.D.: Treatment of War Wounds and Fractures (English version). 1939. Hamilton, Publisher, 90 Great Russell St., W.C., London.

In 1938, he published a record of 605 war fractures, of which 42 were fractures of the femur, without amputations or deaths. In a more recent paper (abstracted in the Lancet, London, December 2, 1939) he states that during the war he treated 1,073 fractures of all sorts by the same principles previously described, with less than 0.75 per cent requiring the premature removal of the plaster encasement because of unexpected complications.

Statistical compilations of the experience of the military surgeons attached to General Franco's armies have not yet been collected in sufficient number for general comparison with the Catalonian statistics, but since the majority of the Spanish surgeons have been influenced by Böhler's teachings, the figures of the Victoria Base Hospital, reported by Captain Arguelles Lopez (Revista Esp. d. Med. y Cirugia de Guerra, 1, September, 1938) are comparable to those of Dr. Jiméno at Banolas. Thus at Victoria (a Franco hospital) there were 252 fractured femurs, with 20 deaths, or a mortality of 7.9 per cent; and amputations 13, or 5.1 per cent.

This experience, I think, is well worth recording, if only as a contrast to the discussion we are now engaged in. Here, everyone is concerned with keeping germs out of wounds, but despite the great progress accomplished, the best minds are still exercising their wits to devise means and methods to keep them out of the atmosphere. There, at the war front, rude experience imposed by necessity seemed to discount the importance of germs, provided the living tissues were allowed to fight their own battle unencumbered by the bodies of dead or dying tissues, and kept undisturbed and protected in the process of repair and reproduction from tempestuous manipulations and destructive germicidal irrigations by absolute fixation in plaster.

It is true that the smell emitted by these patients while their plaster encasements were ripening was somewhat of a shock to sensitive nostrils. But when I saw them get well, with their wounds healed, I realized that "not all cheese that smells bad, is bad."

DR. DANIEL C. ELKIN (Atlanta, Ga., in closing): In answer to Doctor Boland's query as to sterility of the catgut it has been that which meets the requirements laid down by Meleney for sterilization.

DR. FREDERICK A. COLLER (Ann Arbor, Mich., in closing): In answer to Doctor McClure's question whether we took anaerobic cultures or not, I will say that we did not take cultures of this type. The suggestion is an excellent one and it may well be that exposure of the wound to air for 24 hours may play an important part in minimizing or abolishing the growth of anaerobic bacteria.

I am very glad that Doctor Gamble has discussed the paper, as I am sure all of us are indebted to him for the work he has done on the handling of contaminated wounds. For many years, I have followed his advice to leave the wound wide open after severe contamination following operation for acute appendicitis with peritonitis. In the type of wound that I discussed, however, it is highly desirable to preserve an intact abdominal wall if possible and, therefore, we have closed the peritoneum and the fascia, leaving the pack only in the subcutaneous tissues. I wish to emphasize again that we do not feel that this method will be universally successful as it, obviously, will fail in many instances in which the organisms are particularly virulent or in which there is a low tissue resistance. However, we do feel that it may well prevent severe infection in a certain number of wounds that would become infected were they closed in the usual manner.

OPERATIVE AND POSTOPERATIVE INFECTIONS WITH SPECIAL REFERENCE TO AIR-BORNE BACTERIAL CONTAMINATION*

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THE FUNDAMENTAL PRINCIPLES underlying the application of bacteriology to surgery were early recognized as basic; therefore, they have undergone very little change since their introduction by von Bergmann.[1] Refinements and modernization, however, keep these principles constantly before the operating room personnel and tend to make for more accurate and more careful operative technic in the performance of the necessary surgical procedure with a minimum of trauma and without undue prolongation of the operation.

The contamination of wounds by bacteria, aside from those wounds in which, because of the disease from which the patient suffers, bacteria escape into the tissues either from the gastro-intestinal tract or infected regions, may result by direct introduction of bacteria into the wound. It is obvious that the condition of the wound will have a profound effect on the development of these contaminating agents. In this regard a few simple, yet fundamental, facts should be at once obvious. Tissues whose blood supply has been cut off or which have been devitalized by trauma offer an excellent medium for the development of bacteria; live, normal tissue is by nature resistant. For this reason pieces of tissue which are cut off from a blood supply should be removed. If air spaces are present in wounds, either horizontally or vertically, they offer opportunity for accumulation of serum and exudates which furnish an excellent bacterial medium. Wounds which are dry usually do not permit the development of bacteria as rapidly as wounds which are wet; hence, oozing should always be thoroughly controlled.

Aside from these items, which are entirely in the hands of the surgeon, there is another group of important sources of contamination. First and foremost is the introduction of bacteria into the wound. Meleney,[9] in reporting a nine-year study of infection in clean operative wounds, listed the possible sources of contamination in the following order: (a) The nose and throat of the operating personnel; (b) the hands of the operating personnel; (c) the skin of the patient; (d) the air of the operating room; and (e) the instruments and materials used in the operation.

The Nose and Throat of the Operating Personnel.—In 1930, Walker,[11] in studying the incidence of hemolytic streptococcus infections in a hos-

* Read before the Fifty-second Annual Meeting of the Southern Surgical Association, Augusta, Ga., December 5, 6, 7, 1939.

pital in a suburb of Boston, found that in a series of deaths due to hemolytic streptococcus infections following operations on patients who should have had clean wounds, 50 per cent of the nursing personnel of the hospital and three of the six people associated with these operations were carriers of hemolytic streptococci. Following the suspension of operations for a week, the elimination from the operating room of those found to have hemolytic streptococci in the nose or throat and the use of a germ-proof mask worn over both the nose and mouth by most of the personnel, not a single instance of hemolytic streptococcus infection occurred. Another series of wound infections occurred in near-by hospitals; some of these infections were due to hemolytic streptococci. During this epidemic, the results of a study of the customary causes of infection were negative. However, cultures of the nose and mouth of each surgeon, intern and nurse revealed a large number of carriers of hemolytic streptococci. One or more of these carriers had been closely associated with the operation upon the patients infected with the hemolytic streptococci. Walker said: "Again, study of the masks revealed that they were woefully inefficient, as far as they could be considered germ-proof. In the absence of other positive evidence, it seemed fair to deduce that this epidemic of streptococcus infection was probably due to streptococcus carriers inefficiently masked." Walker was, therefore, convinced that direct contamination of the wounds occurred from the nose and throat of the operating personnel.

In studying seven different masks he found that none of them could be considered germ-proof. Walker advised inserting between the gauze meshes a piece of thin rubber similar to that used in rubber gloves; a piece of rubber six inches square is incorporated between two layers of gauze ten inches square. In the upper part of the mask he incorporated a piece of aluminum which could be bent to fit the nose of the individual. He stated that the mask had proved to be germ-proof.

The recent contribution of Hart and Schiebel[7] on contamination of air led these observers to believe that there is a definite correlation between the type and number of organisms found in the air of a given room and in the noses and throats of a group of regular occupants of that room. These authors said that "the number and type of colonies cultured from material taken from the nose and throat seem to parallel more nearly the number and type of colonies cultured from sediment from the air."

The following comment appeared in an editorial on operative sepsis in a recent issue of the British Medical Journal[5]: "Hart's exhaustive studies do not explain how pathogenic staphylococci get into the air of his theatre in spite of all his earlier precautions. These included not only the frequent washing of the room, the provision of filtered air, the wearing of 'large, heavy' masks by all occupants (whether an operation was in progress or not), the exclusion of staphylococcus throat carriers, but even the imposition of silence on all occupants. Any one of the last three of these measures, faithfully carried out, might be expected to prevent contamination of the air from the throats

of the theatre staff; yet, according to Hart, this was the source of infections which continued in spite of adopting all of them."

The Hands of the Operating Personnel.—Devenish and Miles,[4] who studied various sources of contamination of wounds by *Staphylococcus aureus*, placed great emphasis on the rôle played by direct contamination of the wound through needle holes in punctured rubber gloves. These observers found that puncture of a glove was a very common accident. The incidence of puncture in 6,585 patched and unpatched gloves was found to be 24 per cent, while in a second and third series of tests of unpatched gloves worn by surgeons, chief assistants and instrument nurses 14.5 per cent were punctured. The editorial in the British Medical Journal[5] further stated: "The task of Devenish and Miles was made easier by the fact that most of their unexplained sepsis followed operations by a particular surgeon. He was found to be a skin carrier of *Staphylococcus aureus*, and large numbers of these cocci were found in the sweat inside his gloves; they are presumed to have reached operation wounds through small perforations in the glove." It was the opinion of Mr. Devenish and Professor Miles, as well as that expressed by the writer of the editorial, that this was the true explanation of this particular series of wound infections.

The Skin of the Patient.—In spite of all of the labor that has been spent to develop a perfect antiseptic it is not yet possible to apply an antiseptic to the skin and sterilize it completely. Many investigations have been carried out, the sum total of which demonstrate conclusively that by no process yet known is it possible to sterilize the skin completely throughout the layers which are cut by the surgeon's knife. Without wishing to enter into the controversy as to which is the best skin antiseptic, it should be evident that at least three properties should be present in the antiseptic: It should kill bacteria in a reasonably short time; it should not be neutralized by the presence of small amounts of serum, fats, soaps, or oils; and its effect should last at least throughout the operation and preferably for several hours after the closure of the wound. It goes without saying that the antiseptic should not be an irritant to the skin. There are a great number of skin antiseptics which kill bacteria in a short time, but on the basis of the stability of these antiseptics in the presence of protein and their duration of action, the choice is greatly limited.

After many experiments it was decided that the antiseptic which most nearly fulfills the requirements at the present time is tincture of merthiolate; this agent, therefore, has been used in preparation of the skin. In order to test the ability of tincture of merthiolate to act for a long period of time, plates which contained 5 per cent of human serum in agar were exposed in a room occupied by several persons. One-half of the surface of the medium in the plates was painted with tincture of merthiolate. The plates were exposed for four hours, then closed for 12 hours, then exposed for two more hours, after which they were incubated. No colonies grew on the side pro-

tected by tincture of merthiolate while numerous colonies appeared on the other side. This indicated that tincture of merthiolate in the presence of at least 5 per cent of serum will retain its activity for many hours. This is an important consideration in the preparation of the skin.

The Instruments and Materials Used in the Operations.—In 1932, Dandy[3] called attention to the importance of more adequate sterilization in hospitals. He said that in his experience the time generally thought to be satisfactory for sterilization of materials in an autoclave was unsatisfactory and he advocated sterilization in an autoclave for one hour with a constant pressure of not less than 20 pounds. Meleney found that sterilization for 30 to 45 minutes, and prolonging the evacuation time at minus 10 to 15 minutes, was sufficient to kill organisms and spores, whereas prior to his investigation a sterilizing time of 30 minutes at 18 pounds of pressure had been preceded by an evacuation of air just sufficient to reach minus 10 for a few seconds. With this amount of evacuation of air he found that it took an hour and a half to kill test organisms, consistently, in the center of the central drum, and this period of sterilization frequently scorched the materials and softened the gloves. The change in sterilization was followed by inability to obtain growth of organisms from the material autoclaved. It, therefore, is apparent that unless tests are made at frequent intervals to determine the efficacy of the method of sterilization used for autoclaved materials, such materials offer a possible source of wound infection. Mr. Devenish and Professor Miles, in their studies, found that when the skin of a surgeon was infested with *Staphylococcus aureus* the organism would pass through the sleeve of the surgeon's operating gown, if it had been moistened by perspiration or any other cause. Although such source of infection can be indirectly attributed to materials used in the operation, in reality, it is the skin of the staphylococcus carrier. In discussing instruments "sterilized" in antiseptics as a source of infecting oranisms, Meleney said that "the sterilization of sharp instruments such as knife blades, scissors and needles, as well as syringes, buttons, silkworm gut, and catgut tubes has been a real problem. Lahey found that soaking for 15 minutes in 50–70 per cent alcohol, which Meleney states was the former method he had used, was entirely inadequate to destroy even the commonest organisms." Meleney said that "now these instruments are either boiled or soaked in pure carbolic acid for 15 minutes and the Bard-Parker germicide is still being used for the sterilization of the catgut tubes which contain the nonboilable variety of gut."

The Air of the Operating Room.—Since attention has recently been given to air conditioning it is not peculiar that attention should be directed to the possibility of air-borne infection in the operating room. This is the situation which has always been recognized as a possibility but it is fair to state that even to-day a careful evaluation of the facts has not been made. In recent years, a number of attempts have been made to air-condition operating rooms not only in regard to bacterial content but also in regard to temperature

and moisture. Sufficient evidence has been brought forward to indicate that the bacteria in the nose and throat of the operating team and of the gallery have distinct possibilities in regard to the infection of wounds. It is obligatory upon the individuals to cover the oral and nasal orifices with adequate masks. It is further obvious that the operating room should be stripped of all unnecessary equipment and that it should be kept scrupulously clean. It is not too much to expect that the walls, at least as high as the head, and all fixtures should be washed with a damp cloth at least once a day, and that the floor be sponged with a damp mop. Then if the doors and windows are kept closed one should expect that standard plates of agar medium, set in the room in the absence of occupants, will yield not more than five colonies of bacteria per hour, but as the load of the room is increased the number of colonies on the plate will increase. There are other factors which will increase the bacterial content of the room, particularly the site of the room in relation to currents of air and the velocity of the wind outside. Under conditions of dust storms, thousands of bacterial colonies may develop in a single hour on an agar plate in an operating room, and under these conditions the room should be closed except for emergency operations. It is the general property of bacteria that they settle from the upper to lower strata and eventually to the floor. Bacteria which originate in the nose and throat are not often found above the six-foot level and they filter down to the floor. In order to avoid the falling bacteria, which originate in the gallery, from reaching the operating room some surgeons have had canopies built over the operating table. In our own hospital we have for years had canopies built over the instrument tables, and test plates placed on top of and under the canopy clearly reveal the fact that the canopy offers an enormous protection to the instruments.

Professor Cairns,[2] in bacteriologic research at Oxford, studied bacterial infection which occurred during intracranial operations and found that *Staphylococcus aureus* accumulated at the average rate of 0.7 colonies per hour on Petri dishes measuring 9 cm. in diameter (about the same size as the portion of brain exposed) during 27 operations, lasting from one and one-half to 10 hours, the average time being four hours.* Two of the 27 patients died of other causes soon after operation. "Of the remainder, all had first-intention wounds and no sepsis, except two. One of these developed osteomyelitis, due to a *Staphylococcus albus* infection of a bone flap, after a ten-hour operation for removal of a large meningioma of the falx; the infection began in the bone, and there was no trace of infection in the meninges; the bone flap had to be sacrificed before the wound finally healed. The other patient, from whom a frontal astrocytoma was removed, had a first-intention wound and no trace of meningeal infection, but fluid accumulating beneath the galea aponeurotica (removed with an aspirating needle and syringe) showed . . . a growth of *Staphylococcus albus*. This patient made a satisfactory recovery."

* Air was pumped into the operating room through a filter of oil and a wet screen of dettol. Dettol was sprayed into the air at intervals during the operation.

Mr. Devenish and Professor Miles studied the number of bacteria in the air of a standard operating room under ordinary circumstances and found that on a plate 12 square inches in area, approximately the size of the average exposed operative field, 0.3 colonies of *Staphylococcus aureus* appeared per hour. They said: "This is the best available estimate of the continuous risk of infection by *aureus* from the air, though it must vary with the state and staff of the theatre. The area of an operation exposure is usually about 12 sq. in. and the direct settlement on it of one *aureus*-bearing particle every three hours is not an obvious danger." To this they have added, by estimation, the number of these organisms which might have settled on instruments, swabs and gloves and which might be introduced into the wound. They expressed the opinion that the total area of wound and objects introduced into it will not be more than 432 square inches, which is 36 times the area of a plate used for culture. On this basis it is possible that 0.3 times 36, or 11 of these particles, may be introduced into the wound every hour. Mr. Devenish and Professor Miles concluded that if each particle consisted of 20 cocci they would be unlikely to settle in one part of the wound and the odds against an inoculum of 20 cocci getting a foothold in relatively healthy tissue must be high. They said that "the rarity with which very small doses of known pathogens can be made to infect susceptible animals, even after passage, makes it unlikely on *a priori* grounds that *aureus* infection would occur readily in such circumstances. We have, however, no direct evidence on the point. Aside from these speculations we have evidence that the air was not responsible; for, whereas its average *aureus*-content remained constant, the suppuration disappeared, although no attempt was made to prevent the access of air bacteria to the operation wounds. In any event, the constancy of infection at the outset of this investigation suggested a source of *aureus* more constant than the air proved to be."

Professor Cairns said: "Hart,[6, 7] (1937 and 1938), who has made a careful study of the bacteriology of operating rooms, has found that the number of bacteria in the atmosphere varies directly with the number of people present, and he has concluded that the bacteria arise from the noses and throats of the people in the theatre, notwithstanding efficient masking. An alternative possibility exists that the bacteria are present beforehand in particles of dust, and that the presence of the people stirs up the dust. There are evidently considerable local variations in the flora of operating theatres; for example, Hart at Duke University, North Carolina, found as many as 78 colonies of *Staphylococcus aureus* per hour on a plate of blood-agar, and most of his infected cases of thoracoplasty were due to this organism (Hart and Gardner, 1937), whereas in London the highest figure we obtained for *Staphylococcus aureus* was 3.6 colonies per hour, and most of the intracranial infections were from other organisms."

Experiments which we have performed in especially constructed rooms indicate that where proper filtration is introduced into the in-coming air the room may be made essentially sterile, only a few colonies of bacteria develop-

ing on plates exposed for 24 hours. This type of experimentation and practical application has been extensively used by Reyniers, who has raised mammals under completely sterile conditions. His system now in use in the Cradle has demonstrated the low bacterial content of air which can be maintained by proper filtration systems.

Recently, attempts have been made to sterilize the air of the room by the use of ultraviolet rays. It has been known for some time that certain wave lengths in the ultraviolet series will kill bacteria, but it has never been possible to isolate, completely, light waves which will at the same time produce no erythemic reaction of the eyes and skin. For this reason, certain precautions must be taken by the operating force to protect themselves as well as the patient from these rays. Wells and Wells,[12, 13] expressed the opinion that the ultraviolet light sterilizing unit should be directed towards the ceiling and that under these conditions no protection of the eyes or skin is necessary. They endeavor to sterilize the general air of the room, not the specific operative field, as Hart has attempted to do. Hart has suggested that these rays be placed, first, in relation to the field of operation and, second, in certain parts of the room to sterilize the air of the entire room. In spite of several analyses of results which have been obtained, it does not yet appear perfectly clear what the function of these rays has been in the series of cases reported. Certain experiments which we have performed, as well as those performed by the originators of the lamp, suggest that the rays are effective only under the most limited circumstances. For example, Rentschler[10] and his associates, the Westinghouse Electric Company, the originators of the lamp, have stated that the atmospheric dust and grease will coat the glass tubes in which the light is enclosed so quickly, that before each set of experiments is performed the tubes should be wiped with alcohol. The penetration of the rays is clearly stated to be extremely shallow, so shallow, indeed, that a layer of muslin, glass, gelatin, serum, or water will prevent the killing of bacteria. Any solid object placed between the light and the area desired to be kept sterile will result in a failure, since the rays will not travel around or through the solid object. The rays work best in a dry atmosphere, and high moisture content greatly lessens their killing effect. In addition, since the humidity of the operating room must be kept high to prevent static sparks, when inflammable or explosive anesthetic gases are used, the rays are forced to work under the most unfavorable circumstances. The series of experiments which we have performed, in which the bacteria have been coated with a thin layer of gelatin, have resulted in their almost complete protection. This is also true when bacteria are coated with human blood serum. In order to demonstrate quick killing of bacteria, the originators of the lamp have found it necessary to conduct their experiments in small, closed boxes; the bacteria held in suspension in water are sprayed into the box where the light is confined in very close quarters. Even under these conditions, investigators have not been successful in obtaining absolute sterility. As a matter of fact, the experiments show that under the best conditions possible only 90 per cent of

the bacteria are killed. It should be pointed out that these conditions are so artificial that they are never simulated in the operating room, and when one remembers the way the operating field is shadowed by the heads and shoulders of the operating crew it is difficult to see how one can arrange a lamp in such a way that its rays may protect the patient from bacteria which might fall into the wound. Rentschler did not obtain killing of *Staphylococcus aureus* until after 15 minutes exposure at 12 inches from a 30-inch lamp.

Tests which we have performed with the ultraviolet light have indicated that, unless the bacteria are exposed for long periods of time, at close range, to the light, and then without any coating of serum, gelatin, or agar, there is little or no killing to be demonstrated. More or less dry bacteria, exposed in confined regions, are readily killed.

COMMENT.—We should like to quote further from the article of Mr. Devenish and Professor Miles because it expresses an opinion which at the present time seems to be a reasonable one: "A precise definition of the infection risk from the different sources of *Staphylococcus aureus* is impossible. . . . Nevertheless, the staphylococcal history of surgeons A and B in the operating theatre strongly suggests that the main danger lay in the *aureus* infestation of A's skin entering the operative wound through puncture holes in his rubber gloves. Wells and Wells (1936, 1938) have, during the past few years, emphasized the importance of the air as a vehicle of pathogenic bacteria, and Hart (1937) has advocated the sterilization of the air in operating theatres by ultraviolet light. Without minimizing the importance of the Wells observations or denying the efficacy of Hart's method of sterilization, it is questionable whether postoperative *Staphylococcus aureus* suppuration is necessarily due to air-borne cocci. Our experience is limited to one surgical unit, but the striking decline of the sepsis-rate, in the face of a continued *aureus* menace in the theatres, suggests that, in other cases, the improvement due to a greater nicety of operative technic may have been wrongly attributed to the elimination of air-borne pathogens. (To this we might add the apparent superiority of one type of suture material or ligatures over another.) Hart, in his latest report (1938), attributes his avoidance of sepsis to: 'Meticulous operating room asepsis; development of a delicate atraumatic technic; and the use of the least irritating suture material' besides 'the elimination of air-borne contamination.' "

There is no doubt but that the bacterial content of air in an operating room increases with time and the number of persons present, yet no special correlation can be demonstrated between the number of infections and the order of operations performed in any given room. Even yet we do not know the exact source of these bacteria or their significance in regard to wound infection. It is evident, however, that direct introduction of bacteria into a wound by a nonsterile instrument or material, the excretions from noses and mouths of the persons close to the wound, or by sweat from the hands of the operating team through punctures of gloves, are of tremendous significance and an effort should be made first to correct these failures before turning to

the sterilizing of the air of the room. If some effort is indicated in this regard a system of air filtration should be tried but one may not expect to reduce operating room infections greatly until after the first enumerated sources of infection are controlled. Lastly, as has been stated in the British Medical Journal: "If Hart is wrong about the source of infection in his cases but right about the beneficial action of his lamp, does this lamp actually kill staphylococci in the wound itself?" This is a matter which it should be fairly easy to investigate.

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WOUND INFECTION*

A COMPARISON OF SILK AND CATGUT SUTURES

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THE HEALING of a wound is the most important factor in the attainment of good surgery. This is true not only of wounds caused by violence and trauma, but more particularly those made by the surgeon himself. Whipple[1] has stated: "A surgeon's percentage of clean-wound healing is not only a measure of asepsis, but it is an index of his entire surgical philosophy—his knowledge of the principles of healing *per primam*—as well as his attitude towards his patient's welfare and towards the improvement of his art and science of surgery." Although these statements are generally accepted as self-evident, it is to be regretted that the appraisal of end-results by a study of wound healing is rarely carried out. Too often this problem is casually cast aside as of no importance or the surgeon salves his conscience by the easy method of exaggerating his own ability by underestimating his percentage of infections.

In many institutions the importance of the wound is minimized by delegating its closure to assistants and members of the house staff. This is excused on the grounds of haste. Disregard of an essential part of an operative procedure is naturally transmitted by the surgeon to his juniors. Furthermore, the responsibility for the care and healing of the wound is shifted or at least divided, and accurate records of individual operators cannot be obtained.

In order to study wound infections, definite criteria must be set up and careful and scrupulous records must be kept. Five years ago such a study was begun at the Emory University Division of the Grady Hospital. In a book devoted entirely to that purpose, all wounds are classified as clean, potentially infected, and infected. The nature of the operation, the name of the operator, and the suture material are noted. At each dressing, and at the time of the patient's dismissal, a notation is made with respect to healing. Every wound which heals *per primam*—without discharge or exudate from the incision or stitch holes—is marked clean. Those showing even the slightest infection are so classified. Serous exudates and hematomata are cultured and if organisms are recovered, these wounds are classed as infected.

The determination of infection and the record of wound healing is made by the resident surgeon and two assistant residents. Since a greater part of the operations are performed by these men, and since keen rivalry exists regarding the character of their work, it is unlikely that an infection will be

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overlooked, and it goes without saying that they are eager enough to record the mishaps of their seniors. By this method, and by these criteria, it is easy to analyze the character of the work insofar as infection is concerned. The results, thus compiled and openly discussed, have been the cause of much chagrin. This has led to better care of the wound throughout the operative procedure, an improved technic, and a subsequent response in the reduction of infections.

I had long believed that the number of infections was less in wounds sutured throughout with silk as compared to those in which catgut was employed. This was strikingly proved, when the records of the first year were compiled. At that time, catgut was, and still is, the predominant choice of most of the members of the visiting staff. However, members of the resident staff, who have had ample opportunity to use both materials and observe the results, have, without exception, adopted the silk technic, and have enthusiastically continued its use since leaving the hospital. Moreover, the resident surgeons have assiduously trained their assistants in the use of silk, its contraindications, and in the necessary gentle and careful technic in which it should be employed.

The object of this communication is to present statistical data regarding wound healing, and not for the purpose of discussing the merits and disadvantages of different suture materials. It is generally admitted that the period of exudation is shortened and that fibroplasia begins earlier in wounds sutured with silk than in those in which catgut is employed. Furthermore, the liquefaction produced in the absorptive process of catgut acts as a fertile culture medium for bacteria. An excellent account of these matters has been published by Howes,[2] Howes, Sooy and Harvey,[3] Whipple[1] and others. It was the belief that infection was less likely to occur with silk than with catgut that led Doctor Halsted[4] to adopt silk as a suture material in all clean cases. It is only fair to add that his unexcelled records in wound healing were due not alone to the suture material, but to a refined technic based upon complete hemostasis, clean dissection, the avoidance of mass ligatures, undue tension, and meticulous attention to every detail which eliminated tissue trauma.

While the assistants of Doctor Halsted and of Doctor Cushing have for the most part continued to use silk, all insisted that it be employed only under ideal conditions, and have pointed out the possibility of its acting as a nidus of infection. This has led many to abandon its use, although the danger from this source is greatly overestimated. Occasionally when infection occurs a draining sinus will continue until the silk is extruded or removed, but more often healing occurs without removal of the sutures. In five years, there have been only two instances of prolonged drainage from an infected wound, and both healed within six weeks.

Since air-borne bacteria can never be completely eliminated from a wound, it would seem that the technic which tends to limit their growth would be the one of choice, and that silk would, therefore, be preferable even under conditions which were not ideal. Such is the case in the hospital where this

study was made. All the patients were Negroes, and 25 per cent were infected with syphilis. Many were undernourished and anemic. A large percentage of the operations were of an emergency nature. The hospital is old, in a dirty, smoky section of the city, and repairs were frequently being made with resulting dirt and dust. Petri dish cultures, exposed to the air some distance from the operative field, showed 25 implantations of pathogenic organisms after exposure to the air for ten minutes. The rooms were not air-conditioned. The nursing service was entirely by Negro pupils, and a medical student was a member of the operating team in nearly all cases. Ninety per cent of the operations were performed by members of the resident staff, but it is only fair to add that their percentage of infections was less than that of the visiting surgeons. The record and comparison of operations with silk and catgut sutures for the last five years is shown in Table I.

TABLE I

COMPARISON OF OPERATIONS BETWEEN SILK AND CATGUT LIGATURES

Clean Cases

	Silk			Catgut		
	No. of Cases	Infected	Per Cent	No. of Cases	Infected	Per Cent
1935	81	1	1.2	147	25	17.0
1936	125	4	3.2	154	12	7.8
1937	217	9	4.1	143	6	4.2
1938	452	7	1.5	74	6	8.1
1939	317	4	1.2	77	7	9.1
Totals	1,192	25	2.1	595	56	9.4

It is noted that the percentage was higher in 1937 than in other years. This might be attributed to some controllable cause such as faults in sterilization. However, it was actually due to the high percentage of infections which occurred in the patients of one operator, and the blame must, therefore, be placed in his hands.

It has been stated, and with good reason, that results are frequently better with silk than with catgut because in the employment of the latter large sizes are employed. Furthermore, it has frequently been pointed out that surgeons employing silk are apt to be more careful throughout the whole procedure than when catgut is employed. In this study neither of these factors is applicable. Catgut No. 00 and No. 0 were the sizes generally employed, and the same operators for the most part employed both suture materials.

Noting the marked difference in the wound infections in clean cases, the use of silk has been gradually increased in those wounds which were considered, potentially, but not grossly, infected. These wounds have been studied and compared in a similar manner. They include compound fractures of the skull and long bones, wounds of the heart and chest, wounds of the abdomen without intestinal perforation, gangrenous appendicitis, *etc.* The comparative results in this group are shown in Table II.

TABLE II

CASES POTENTIALLY INFECTED

(1935–1939)

Silk			Catgut		
No. of Cases	Infected	Per Cent	No. of Cases	Infected	Per Cent
188	15	7.9	312	77	21.4

CONCLUSIONS

(1) A comparative study of clean wounds sutured with silk and with catgut is given.

(2) Rigid criteria in the determination of infection are necessary.

(3) With silk, infections occurred in 2.1 per cent of the cases, as compared to 9.4 per cent in those where catgut was employed.

(4) In potentially infected cases there was likewise a marked difference —7.9 per cent of the wounds sutured with silk were infected as compared to 21.4 per cent in those cases where catgut was employed.

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GRADUATE TEACHING OF SURGICAL PATHOLOGY

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THE REQUIREMENTS of the various Boards set up to pass upon the fitness of graduates in medicine to become specialists in those fields which have to do with surgery and allied arts, demand a certain amount of training in pathology and more particularly in surgical pathology. In the well-established hospitals, where there are Resident systems for specialty training, a variable amount of time is allotted for this purpose, and graduates of these institutions are usually properly qualified in this respect. But there are not enough such institutions to train the number of men required, and the Resident system does not solve the problem of the many graduates now practicing specialties who wish to become licentiates by qualifying for and passing the examinations of the various Boards. Recently, Graham[1] focused attention upon the lamentable ignorance of surgical pathology displayed by a number of candidates who appeared before the American Board of Surgery. It is safe to conclude, therefore, that there is a very real problem to be met.

The Laboratory of Surgical Pathology at Columbia University has been profoundly affected by this demand. There has always been a certain number of volunteers, not officially connected with our institution, working in the laboratory because they wished to gain greater familiarity with the pathology of surgical diseases, but in recent years the number of such volunteers has increased inordinately so that we are not able to accommodate all of them. Since the effective factor is national, a similar condition must prevail in all parts of the United States. For this reason, I believe it will be in order to report upon the way in which we have organized our facilities to meet the needs of these men.

Before doing this, it will be necessary to point out certain features which characterize the study of surgical pathology. It is the branch of pathology which deals with the study of disease processes as they occur in the living. This has the advantage of permitting the observation of lesions at an early stage, when they may be reversible, but there is also the disadvantage of not allowing the examination in detail of the body as a whole. This lack has to be filled as well as may be by completing the picture with an interpretation of the symptoms, the physical signs and the other laboratory data. Thus, surgical pathology is not a pure science but a branch of clinical medicine. This conception has guided us in planning the activities of those who come to our laboratory to study.

We do not accept volunteers for less than three months but set no other limit to the length of their stay, and a number of men have remained a year

or more. During their sojourn in the laboratory they are required to devote to it a major portion of their time. During 1939, there were 20 workers in the Laboratory of Surgical Pathology in addition to its regular staff. Ten of these were members of the resident staff of the Presbyterian Hospital from the Departments of Surgery, Otolaryngology, Radiology and Pathology, and ten were volunteers.

The work consists basically of a detailed description of the gross and microscopic features of the surgical material and an interpretation of it. This is supervised by the Resident Surgical Pathologist when necessary. The workers are required to familiarize themselves with the clinical aspects of the cases assigned to them and also to keep in touch with all of the cases on the surgical wards by attending the surgical rounds each morning. At the weekly surgical staff meetings, which they must attend, they have an opportunity from time to time of demonstrating the salient features of some instructive specimen. Once a week there is a surgical pathology conference where cases involving difficult diagnostic and therapeutic problems are considered. The clinical history of a case is read, the microscopic preparations are studied, and each participant is asked to express an opinion about the diagnosis and sometimes the treatment. The discussion is concluded with comments by one of the senior surgical pathologists present. These conferences are often attended by other pathologists and radiologists who serve to broaden and increase the interest of the discussions.

Once a month the surgical pathology group holds a joint conference with the radiologists and radiotherapists at which cases of neoplastic and allied diseases involving difficult problems in diagnosis and treatment are jointly considered. The histologic features of each case are projected on a screen and commented upon by one of the senior surgical pathologists.

One day each week the workers attend the Neoplasm Clinic. This is conducted by a group composed of surgeons, radiotherapists and surgical pathologists. The volunteers work up the cases, present them, and then hear the treatment discussed and see the results in follow-up cases.

The third year medical students are given instruction in surgical pathology once a week during a two-hour period. This consists of lectures, the examination and description of gross material and the study of microscopic preparations. The volunteers participate in this instruction by supervising the students' laboratory work.

Finally, those volunteers who demonstrate special aptitude are encouraged to undertake the solution of small problems in surgical pathology.

This program, then, permits the worker to prepare the description of the specimen which will become part of the hospital record, to correlate the lesion with the clinical aspects of the case, and to participate actively in teaching, group discussions, and presentations to the surgical staff. Decidedly, not the least of his privileges is that of enthusiastic and intelligent discussion of current surgical and allied problems with his fellow workers.

The organization of a program for teaching surgical pathology to graduates must of necessity be varied, depending upon the facilities available. However, the writer is convinced that it is essential that it be guided by two principles: First, that the worker shall personally examine and report upon fresh surgical material, and, second, that he shall always correlate it with the clinical features.

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BRIEF COMMUNICATIONS AND CASE REPORTS

TOE TO FINGER TRANSPLANT *

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THIS is a clinical series of one case of a toe to finger transplant given as a reintroduction after a six years' absence from our program. The case reported is of a young child who through an accident had lost the distal part of her middle finger of the right hand. The parents' urge that we do something for her was most emphatic.

This is not presented with the idea that it is anything new, but employment of the plan is not likely of common occurrence. It seemed particularly fitted to the needs of the case in hand—restoration of the distal segment of a finger of a young female child. If performed solely for the sake of appearance, such an operation would fall short of its purpose if more than one joint were missing, except possibly on the little finger, where two phalanges might be replaced without attracting attention, using the second toe, but to do this the pedicle of the carrying flap might have to extend up on to the dorsum of the foot. It is also conceivable that the great toe could be substituted for the distal and part of the proximal phalanx of the thumb, this for utility as well as appearance. A partial restoration of the little or the fourth finger might add to the usableness of a hand that had lost the three inner fingers, provided either of the two inner metacarpophalangeal joints had been spared to serve as a base for the transplant. If successful, this should facilitate the grip on the handle of a mechanic's tool or a golf club.

In a young subject, the natural difference in appearance between a finger and a toe would be less accentuated by shoe wearing, while the three or four weeks of the unnatural body and limb position would cause less discomfort and be less apt to cause arthritic changes. These could be lessened by a preoperative practice in the unnatural position.

A girl would be more likely to be distressed by the deformed finger than would a boy or man. The hope that sensation, tactile, heat, cold, *etc.*, will ultimately be restored without having performed direct nerve suture is based on its reappearance in almost all transplanted flaps, usually within nine months. A direct nerve suture would add another step to a somewhat complicated operation. Doctor Byars contrived a laced-on, thin leather jacket in which was incorporated a palmar finger-bar fixed to a tailor's thimble. This is to

* Read before the Fifty-second Annual Meeting of the Southern Surgical Association, Augusta, Ga., December 5, 6, 7, 1939.

be worn constantly over a knitted or kid finger-stall until normal sensation of the transplant is regained, in order to prevent burns or other injuries.

Figure 1 shows the hand bound to the foot, but note that the knee was held in extreme flexion and that, also, the forearm and lower half of the arm were bound to the leg and thigh by supposedly nonirritating adhesive tape.

Operative Procedure.—After making a dorsal slit on the toe, from the center of the second phalanx back to the foot, and removing its proximal and half of the second phalanx, and then making a guillotine disarticulation of the finger stump, the cartilage was scraped from the head of its second phalanx. It also shows that the mobilized distal part of the toe and proximal part of the finger were sutured two-thirds around and to permit this, the original dorsal toe incision had been extended forward, as two arms of a

FIG. 1.—A sketch showing the hand superimposed upon the foot.

Y, one to each side of the distal toe joint, thus inclosing an undisturbed dorsal triangle of skin and subcutaneous tissue. This latter was fitted into a dorsal slit made over the end of the finger. Also, about one-third of the transversely cut end of the finger-covering on each side was tacked to the contiguous border of the spread-out distal part of the dorsal toe slit. On the finger, the tendons had been divided at the joint level, and on the toe, 3 Mm. proximal to the bone cut off the middle phalanx. The tendons, front and back, were united with three No. 000 silk sutures. Bone fixation was accomplished partly by having these tendon sutures engage also the fringe of joint capsule that had been left surrounding the head of the finger phalanx and on each side this bit of capsule was attached to apposing deep tissues on the toe. The now boneless proximal one-half of the toe thus formed a mobile pedicle long enough to allow the distal half to move dorsally into the axis of the finger. This pedicle was divided four weeks later, after carefully

figuring how much of it was needed for the finger and how much would then remain to cover the site of the toe disarticulation. The latter was closed immediately, but on account of some inflammatory thickening on the finger, we here trusted to the healing to draw together the unsutured bordering

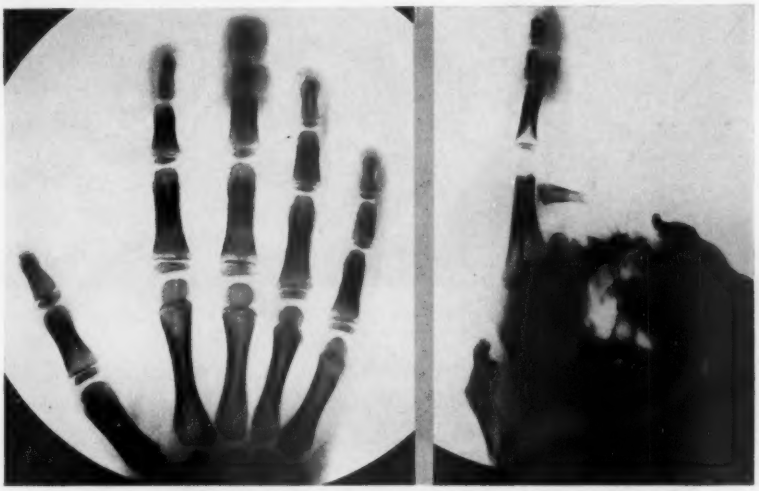
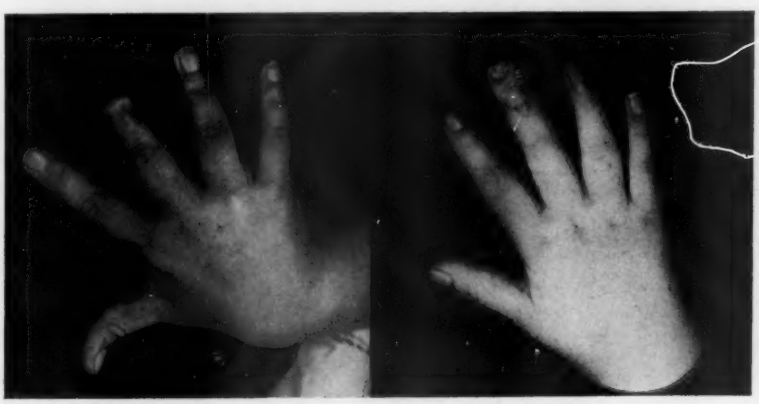


FIG. 2.—Roentgenogram of the fingers, six weeks after the initial transplantation, showing the inflammatory thickening of the transplant.

skin edges. This required about two weeks, but it ultimately made a smooth surface union.

Figure 2 shows roentgenograms, taken approximately six weeks after the initial transplantation, which demonstrate the inflammatory thickening



A B

FIG. 3.—Photographs (A) showing the preoperative condition; and (B) the cosmetic result 48 days after primary union.

of the transplant, but its color and circulation at this time were, apparently, perfectly satisfactory. The only other evident abnormality on the films is that the finger appears to have four phalanges.

Figure 3 shows the preoperative condition and also the result 48 days after primary union.

Figure 4 is a comparison in appearance of the natural with the reconstructed hand.

FIG. 4.—Photograph showing the comparative appearance of the natural with the reconstructed hand.

Figure 5 shows that the transplanted joint now remains straight while the fingers are naturally flexed, but she has here already developed a discernible amount of voluntary flexion and extension. We have reason to hope these

FIG. 5.—Photograph showing the functional result. Note that the transplanted joint remains straight while the fingers are normally flexed.

movements will ultimately approach a normal range when, in time, the fine silk sutures loosen that now still fix the already united tendons to the residual fringe of joint capsule that was retained at the site of union.

TRANSPLANTATION OF TOE FOR MISSING FINGER*

END-RESULT

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Case Report.—M. L., white, female, age 7, came under observation in Mount Sinai Hospital, in July, 1922. Deformities of the fingers of both hands were noted at birth, and also fusion of two toes of the left foot. The hands were useful for ordinary purposes. The right hand presented the chief problem for improvement of the deformity and of function. The thumb, fourth, and fifth fingers were normal. Only the proximal phalanx of the index finger, with its thickened surrounding tissues, was present. The middle finger was totally absent, a short stump of the proximal phalanx, about 1 cm. long, projecting beyond the head of the metacarpal bone. The plan was to transplant the second toe of the right foot with part of the metatarsus in the form of a pedicled graft. The metatarsus and adjacent tissues were to be included in order to supply the necessary length. A few days before operation, a plaster of paris mold was prepared to hold the child in position with the right knee flexed and the right arm extended downward in front of the body.

Operation: The stump of the missing finger was first prepared. The overlying skin was reflected as a flap, with its base on the ulnar side. The shell of proximal phalanx, found to be of cartilaginous consistency, was exposed and its end freshened. The stumps of the flexor and extensor tendons of the missing finger were exposed and dissected free for a distance of about 2 cm. A wet pack was placed over the hand and dissection of the foot was begun. This consisted in an incision across the web between the first and second toes and extension of the incision over the dorsal and plantar surfaces of the foot. The head of the second metatarsal and the flexor and extensor tendons of the second toe were isolated and were divided about 1.5 cm. back of the head of the bone. The tissues on the lateral aspect of the second toe were not disturbed, so that the toe with its adjoining metatarsal bone and tissues swung on a thick pedicle, with undamaged lateral nerve and blood supply. The hand and foot were then brought together by rotating the right leg and bringing the shoulders forward. The problem of adjusting the fingers to the foot was, however, more difficult. The thumb and second finger were placed on the dorsum of the foot, and the fourth and fifth fingers over the sole of the foot. After the hand and foot were placed and held in position, the stump of the finger was approximated to the pedicled toe. A suture of chromic gut was passed through the shell of the phalanx of the missing finger and through the metatarsal bone and tied without tension. The ends of the extensor and flexor tendons of toe and finger were approximated with fine silk. The margin of the skin flap of the finger was sutured to that of the toe. Immobilization was effected by a plaster of paris encasement.

In recovery from the anesthetic the child struggled and the plaster shifted. Some separation of the skin was noted on the third day, and it was necessary to apply adhesive straps to maintain approximation of the skin. The circulation in the pedicled toe remained good.

The detachment of the toe was undertaken 15 days after the first operation. An incision was made across the web between the second and third toes and extended wide

* Presented before the New York Surgical Society, April 26, 1939. Submitted for publication, July 7, 1939.

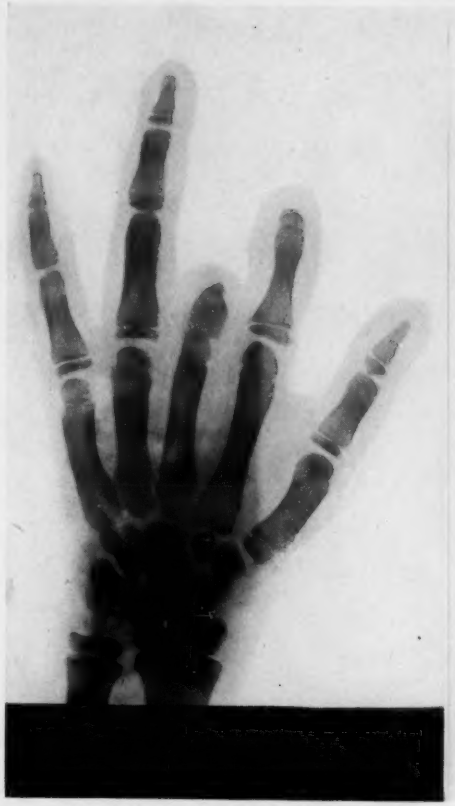


FIG. 1.—Roentgenogram of hand before operation.

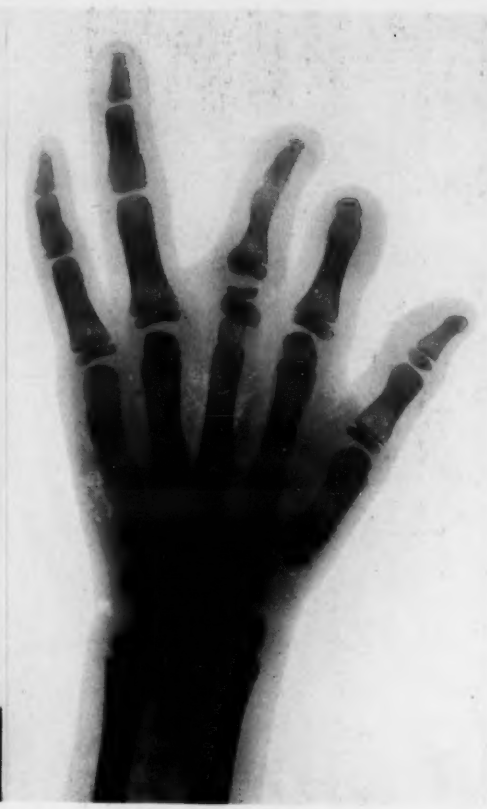


FIG. 2.—Roentgenogram of hand taken several years after operation.

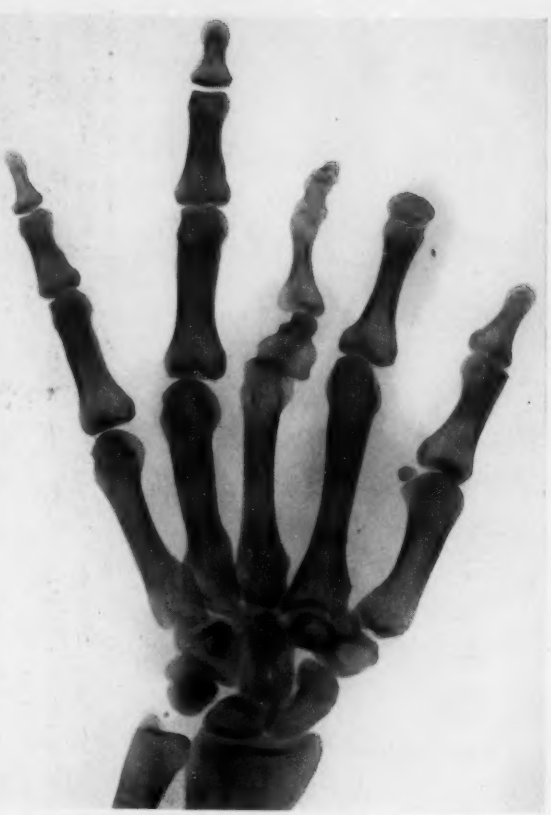
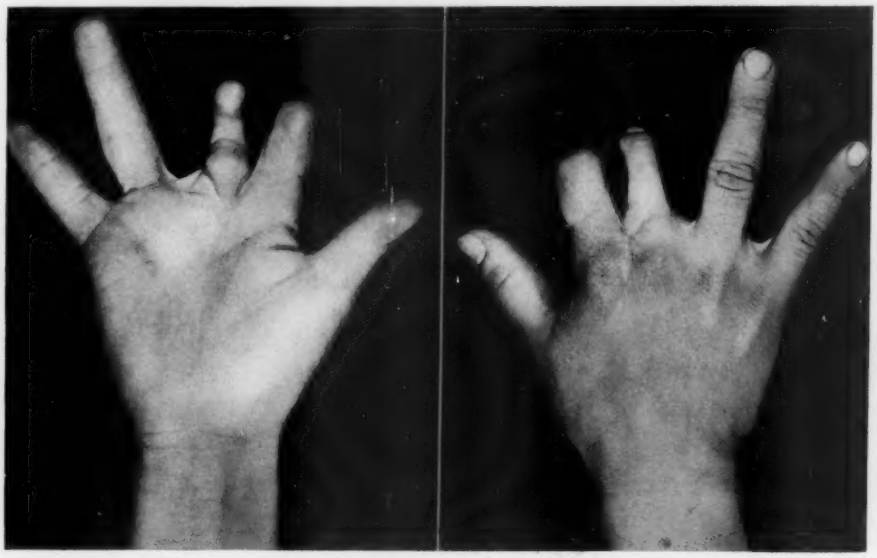


FIG. 3.—Roentgenogram showing present status. Note the viable phalanges in the graft as well as the increase in size in the stump of the proximal phalanx of the missing finger.

of the second toe, so that there would be more skin than was necessary. The space in which the dissection was made was cramped and the tendon anastomoses were damaged when the toe (with adjoining metatarsal tissues) was completely detached. It was necessary to remove much of the fat pad on the plantar surface and part of the metatarsus of the transplant, because these structures made too pronounced a prominence for a cosmetic result. The skin margins were trimmed and sutured.

Subsequent Course: The circulation remained good in the graft from the outset. The wound healed by primary union for the most part. Sensation was first noted in that part of the graft nearest the finger stump about three weeks after detachment. It advanced in ring-like fashion and sensation was normal about six months after operation.

There were never any symptoms referable to the transplanted toe. About six weeks after operation, it appeared certain that the tendon sutures had not held. Consent for secondary suture of tendons could not be obtained. During the first winter following



A B

FIG. 4.—Photographs of transplanted toe at present time. A. Palmar view. B. Dorsal view.

the operation, the transplanted toe was colder and more bluish than the adjoining fingers in cold weather. These manifestations have subsided since that time. The only disturbance in nutrition of the grafted toe was to be noted in the nail. This grew irregularly at first. During the early years it grew more slowly than normal, and the free margin of the nail broke off from time to time.

The function in the transplant is limited to movements transferred to it by the adjoining stump of the finger. Separate motions can be anticipated only if the tendons are sutured or a tendon transplant performed. The roentgenograms show not only survival of the phalanges, but also indubitable evidence of increase in length and thickness. This is most clear in the proximal phalanx of the grafted toe. At no time after operation, in a period of one year during which numerous roentgenograms were taken, was there any evidence of absorption of the phalanges with bone replacement, a phenomenon that had been anticipated. There was a slowly progressive increase in the length and thickness of the transplanted toe until adult life.

End-Result.—Seventeen years have elapsed since operation. The end-result is a permanently viable transplant with normal circulation and growth. The cosmetic result is fair. The functional result is *nil*, because the tendons of the graft were not sutured to the tendons of the stump of the finger.

SUPPURATIVE THROMBOPHLEBITIS OF THE FEMORO-ILIAC VEIN WITH BLOOD STREAM INVASION

CASE REPORT

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Case Report.—H. B., male, age 67, was struck by a locomotive, May 8, 1938. He suffered a severe mangling of the left lower leg and was taken to St. Joseph Hospital, where a disarticulation at the knee was performed.

Postoperatively, he improved steadily, but the stump was unsatisfactory due to gangrene of the soft tissues covering the end. Six weeks after the first operation, the lower end of the femur was amputated and a new stump constructed, which was drained. A moderate degree of infection developed, but by July 17, 1938, had cleared up considerably and the patient was able to be up and about on crutches.

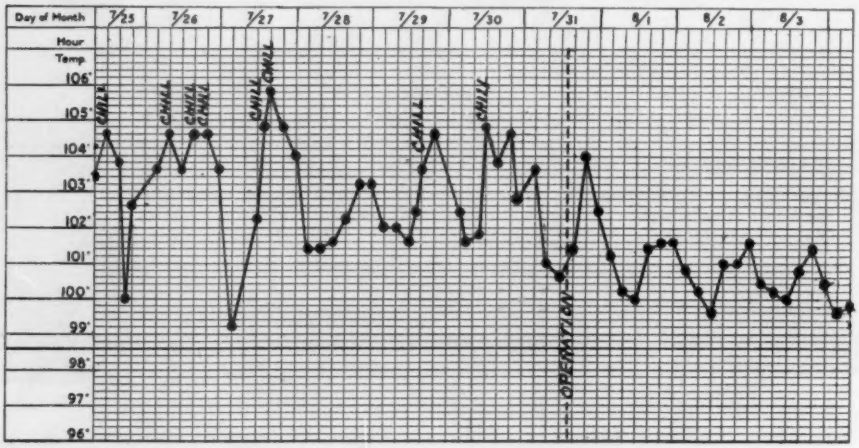

CHART 1.—Showing four-hour rectal temperature curve from time of first chill to fourth postoperative day.

Suddenly, on July 25, 1938, after being home eight days, the patient had a severe chill followed by a high temperature (Chart 1). The chills and high temperature continued to recur and were followed by profuse sweats. Within a few days, the stump became markedly swollen with pitting edema, and a blood culture, July 27, 1938, showed a heavy growth of *Staphylococcus aureus*. A diagnosis of suppurative thrombophlebitis of the left femoro-iliac vein with blood stream invasion was made; and scattered râles in the lungs suggested the presence of metastatic foci. On July 31, 1938, six days after the first chill, he was readmitted to the hospital.

Operation.—Under spinal anesthesia, a vertical incision was made in the abdomen, extending from the level of the umbilicus downward over the middle of the inguinal ligament. The abdominal cavity was opened low and the peritoneum raised over the region of the left iliac vessels. The left external iliac vein was easily identified and was felt as a firm, noncompressible cord. It was followed proximally to its juncture with the hypogastric branch, just distal to which it abruptly became soft and compressible. It was felt that we were now above the level of the thrombus and at this

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point two ligatures of braided silk were applied separately. The thrombotic area of the vein was left intact, being merely overlayed, retroperitoneally, with strips of iodoform gauze which were brought out from the lower end of the wound. The incision was closed in the usual manner after repairing the opening made in the peritoneum.

Subsequent Course.—Postoperatively, the temperature rose to 104° F., but was unaccompanied by a chill (Chart 1), and by the next morning the general picture had entirely changed. The patient now appeared convalescent instead of moribund as before the operation. Thereafter, the temperature continued at a low level and the chills did not recur.

Following removal of the drain, there was a moderate amount of purulent discharge for several weeks. The edema of the stump spread upward nearly to the axilla at first, but later receded and eventually disappeared almost entirely. Other postoperative complications included a superficial thrombosis in the other leg from infection at the site of his transfusion; wound in the ankle; also a cystitis; and a persistent arthritis of the right shoulder. In spite of these setbacks the patient's strength gradually returned, and he was finally discharged from the hospital, September 24, 1938, 19 weeks from the date of the accident.

COMMENT.—Thrombophlebitis of the infectious and suppurative types constitutes only about 3 per cent of the thrombophlebitides.[1] There is, however, a very high mortality because of the frequency of septicemia and metastatic foci. This high mortality, as recently shown by Rosenow and Brown,[2] varies directly with the inability of the surgeon to check blood stream invasion from the septic focus.

The idea of trying to stop the spread of infection from a diseased vein into the general circulation apparently originated with John Hunter,[3] who, in 1793, advised that a "compress . . . be put upon that part of the vein just above the suppuration." In 1865, Henry Lee[4] applied this principle and used a ligature for the first time in two of four cases.

In 1878, Kraussold[5] reported a case of femoral suppurative thrombophlebitis, successfully treated. The patient, a male, age 29, had had an amputation through the condyles of the left femur. Four days later, a severe chill and high temperature developed and the stump was explored. The femoral vein was found to contain a purulent thrombus and was ligated at the level of the inguinal ligament.

In 1884, Zaufal[6] tied off the internal jugular vein in an instance of lateral sinus thrombophlebitis following suppurative otitis media, and, in 1900, Viereck[7] showed statistically the value of this treatment. In 1902, Trendelenburg[8] reported ligations of the ovarian and deep pelvic veins in puerperal sepsis; in 1909, Wilms[9] ligated the ileocolic angle radicles of the portal vein in appendicitis; and, in 1912, Bullock[10] ligated the facial veins in a case with a carbuncle of the upper lip.

The femoro-iliac vein is a frequent site of thrombosis, but only very rarely is the clot infected.[11] When infection does take place it may be hematogenic,[12, 13, 14] but is usually due to direct extension from a septic focus as in the present case.[15, 16, 17]

The diagnosis of suppurative thrombophlebitis with blood stream invasion

is easily made, as a rule, by the recurrences of severe chills and high temperatures. Often chills are absent, however, and the temperature curve may not be typical.[18] Edema, of course, helps to locate the area involved. Blood cultures are said to be usually negative.[18, 19]

Some cases undoubtedly subside without surgical interference, but just how long a case may be treated expectantly cannot be told in advance. Probably a positive blood culture should stimulate active intervention, though waiting for the report might cause serious loss of time. Above all, it should be emphasized, that as long as the patient lives, even though a week or more may have elapsed since the first chill, operation may still offer a good chance of recovery.

SUMMARY

A case of thrombophlebitis of the femoro-iliac vein secondary to amputation of the femur is reported. Simple ligation of the iliac vein was followed by rapid, marked improvement and eventual recovery. It is concluded that in this type of case, even though the patient may appear *in extremis*, operation is indicated.

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CONGENITAL, PEDUNCULATED PSEUDOPAPILLOMA OF ANUS

CASE REPORT

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MALDEVELOPMENT of the proctodeum and distortion of the perineal raphe are among the more common types of congenital anorectal deformities. Such variations from the normal have appeared in eight (66 per cent) of our 12

FIG. 1.—Photograph showing the thickened perineal raphe merging with the base of the pedicle.

cases of anorectal malformations. In our group, this type of deformity was not limited to those cases where the occlusion was due to a simple imperforate anus (Group III, Ball,[1] Group II, Berman,[2] Ladd and Gross[3]), but occurred in some of the other classifications as well. Although improper development of the proctodeum and perineal raphe is not an unusual deformity, it is rare for such a malformation to manifest itself as a pedunculated growth. A care-

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ful search of the recent literature fails to reveal any description or reference to the type of anomaly presented in this report. Because of the simplicity of the surgical measures necessary for correction as well as the lack of functional impairment, only a brief résumé of this case is given.

Case Report.—This infant was seen, November 1, 1937, in consultation with Dr. Rollin Kuebbeler, who had delivered the child five days previously. At that time he noted the presence of the pedunculated growth which in no way interfered with normal anal function. Examination revealed a patent anal orifice of normal dimensions. The median raphe was thickened, extending from the base of the scrotum across the perineum to the anterior aspect of the anus. At that point, the thickened epidermis veered to the left and at the lateral border was continuous with the pedicle of the tumor. The pedicle was about 4 cm. long and the ovoid tumor measured 3x4 cm. (Fig. 1). Both were covered by what appeared, grossly, to be normal epithelium. Since no associated malformation was present in the anal area or elsewhere, we advised surgical removal of the growth. Doctor Kuebbeler, after infiltrating the base with 0.5 per cent procaine, ligated the pedicle at the left lateral anal margin and excised the tumor. Healing progressed in a normal manner and the deformity was satisfactorily corrected.

FIG. 2. FIG. 3.

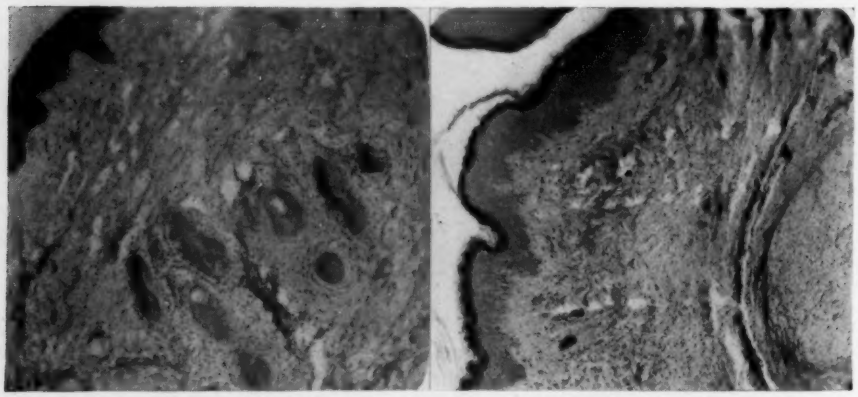

FIG. 2.—Photomicrograph showing normal structure of skin, subcutaneous, connective and fatty tissues. A few hair follicles and sebaceous gland ducts are present. (×100)
FIG. 3.—Photomicrograph showing a large nerve running through the pedicle. (×100)

Sections from the tumor were examined by Dr. Thomas L. Ramsey, Toledo, Ohio, and Dr. Carl V. Weller, Ann Arbor, Mich. A summary of their reports states: The diagnosis is that of a congenital, pedunculated pseudopapilloma with fibrolipomatous structure and with a definite well-formed epidermis (T. L. Ramsey). The specimen is not a true neoplasm but a developmental anomaly consisting of a pedunculated mass of adipose tissue covered with a fairly typical corium and epidermis (Figs. 2 and 3) (Carl V. Weller).

Sir Arthur Keith[4] said: "Surgeons are apt to regard embryology as a subject which has little direct bearing on their art . . . the opposite is the case, that all the changes which bring about the development of the body are instances of superb surgery. Parts are perfectly opposed and, as a rule, exact and orderly union occurs in a manner in which surgeons may dream of but can hardly hope to attain in practice." Thus, the congenital origin of this

growth can best be understood from a brief résumé of the embryology of the anus and perineum. Shortly after the third week of embryonal life the proctodeum invaginates to form the site of the future anus. This ectodermal depression deepens and approaches the descending termination of the blind gut. As these near each other, the intervening mesoblast is obliterated in such a manner that the resulting septum is formed by the entodermal wall of the rectum and the ectodermal epithelium of the proctodeum. This membrane is absorbed and, at about the eighth week, there is normal communication between the anus and rectum. During the second month, the urogenital septum extends to the surface to form the perineal body and, after the beginning of the third month, the outer genital folds coalesce to form the perineal raphe. According to Keith, it is because of the late period of union that so distinct a raphe or scar is left along this line of fusion. Although the cause of these defects is unknown, he offers the interesting hypothesis that the factors producing this scar are of the same order as those preventing the union of ordinary wounds.

Upon reviewing this embryologic process, it is found that failure in the normal development of this area may result in: (1) The persistence of a partial or complete membrane in the anal canal; (2) a superficial band of skin partially or completely obstructing the anal orifice; or (3) an unbroken and thickened median raphe covering the outlet. It is a matter of conjecture whether the deformity under discussion had its origin in improper proctodeal development or in a variation from normal of the perineal raphe. The salient points about this anomaly are: (1) The presence of a patent anal orifice of normal dimensions; (2) an unusually thickened perineal raphe extending from the scrotum to the anus; and (3) a pedunculated tumor arising from the anal margin and apparently continuous with the raphe. By interpreting these factors from the embryologic standpoint, we feel justified in assuming that the proctodeum developed in a normal manner except for the persistence of the deformed raphe. This latter, instead of remaining in the midline to partially obliterate the anal orifice, deviated to the left to form a pedunculated tumor. Upon this basis, we may conclude that the anomaly under discussion is one of the more common congenital anorectal deformities which has assumed a bizarre and unusual form.

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ENTEROGENOUS CYST

OBSERVATION OF AN UNUSUAL PHYSICAL SIGN

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THE FOLLOWING CASE is reported not only because of the rarity of the condition, but also because of the observation of an unusual physical sign on examination of the patient:

Case Report.—University Hosp. No. 652337: S. B., white, female, age two, was admitted to the University of Minnesota Hospital September 21, 1936. The mother noticed that when the patient was five or six weeks old, the baby's abdomen was more rigid or "tight" on the right side. When the patient was one year old, the mother felt a mass in the right side of the child's abdomen. This mass had gradually increased in size until six months before admission. Five weeks before coming to the hospital, the patient began to complain of pain at times in the region of the umbilicus.

The past and family histories were essentially negative except for occasional attacks of tonsillitis. The child's appetite was good. There was no history of intestinal colic, bloody stools, diarrhea or constipation. Cardiorespiratory and genito-urinary histories revealed nothing of note.

Physical Examination.—Negative except for a large tumor in the right lower quadrant of the abdomen. This mass was round, movable, not tender, and was apparent on inspection (Figs. 1 and 2) and moved on respiration. It was dull on percussion. No borborygmi were heard on auscultating the abdomen. Most interesting of all, however, was a finding first observed by Dr. W. T. Peyton of the Department of Surgery, namely, the mass seemed to have contractile properties, as at times its consistency would change from soft to hard and then become soft again. The liver and spleen were not palpable. Rectal examination revealed a mass which could be pushed into the pelvis, but which was extrinsic to the rectum.

Laboratory examination of the blood and urine was negative. Wassermann reaction was negative. Roentgenologic examination of the chest and intravenous urograms were normal. A barium enema revealed a mass on the right side of the abdomen displacing the bowel to the left and posteriorly. There was no roentgenologic evidence of an intra-abdominal hernia. *Clinical Diagnosis:* Mesenteric or omental cyst, or possible intra-abdominal hernia.

Operation.—September 29, 1936: Under ethylene and ether anesthesia, the abdomen was opened through a right midrectus incision. A large cyst was seen in the right lower quadrant. The mass could not be delivered out of the abdominal incision. It was about four and one-half inches in diameter, thick-walled, and light in color. Large blood vessels coursed over its surface. At this time it was difficult to determine the exact connections between the cyst and the intestine. A needle was inserted into the tumor and approximately 200 cc. of mucoid, grayish, transparent fluid was aspirated. It was then possible to lift up the entire mass and deliver it through the abdominal incision (Fig. 3). The cyst was in the angle between the cecum and terminal ileum, and the central portion of the attachment seemed to be at the superior angle between the ileum and cecum. On attempting enucleation, it was found to be intimately adherent to the wall of the ileum.

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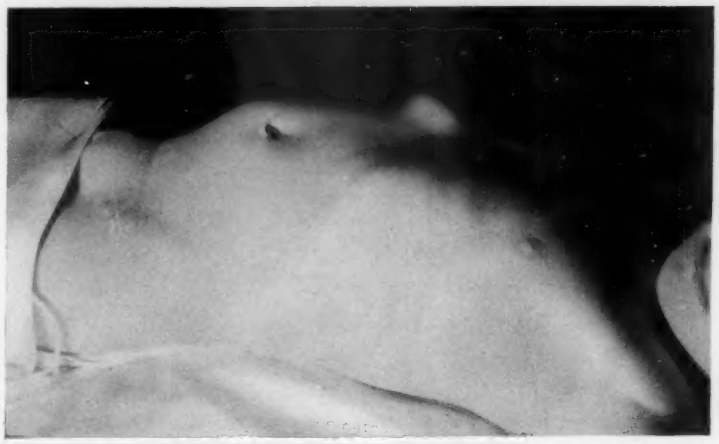
The cyst was opened and the inner lining dissected out of the thick-walled sac. The inner lining was granular and about 1 Mm. in thickness. The outer portion of the wall was 3.5 Mm. thick and had the appearance of muscular fibers. After the entire lining

FIG. 1

FIG. 2



FIGS. 1 and 2.—Front and side views of the patient's abdomen showing the tumor mass on the right side.

was removed from the sac, the major portion of the outer wall was then excised and the adherent portions sutured together to make a much smaller closed space. The appendix

was normal. The terminal one and one-half inches of the ileum were dilated. The cecum was not dilated nor was its muscular wall thickened.

The impression at operation was that this was an enterogenous cyst arising from the wall of the terminal ileum.

Examination of the fluid aspirated from the cyst revealed it to be sterile. Specific gravity 1.010, containing 1,300 white blood cells. Sugar 54.5 mg. per cent, protein 22.6 mg. per cent. There was no mucus.

Pathologic Examination.—Gross: The cyst measured 8x10 cm. The wall was thick and contained muscle. The inner lining was smooth; there were no papillary ingrowths. *Microscopically* (Path. No. HO–36–3190), a smooth-walled cyst was found, lined by a

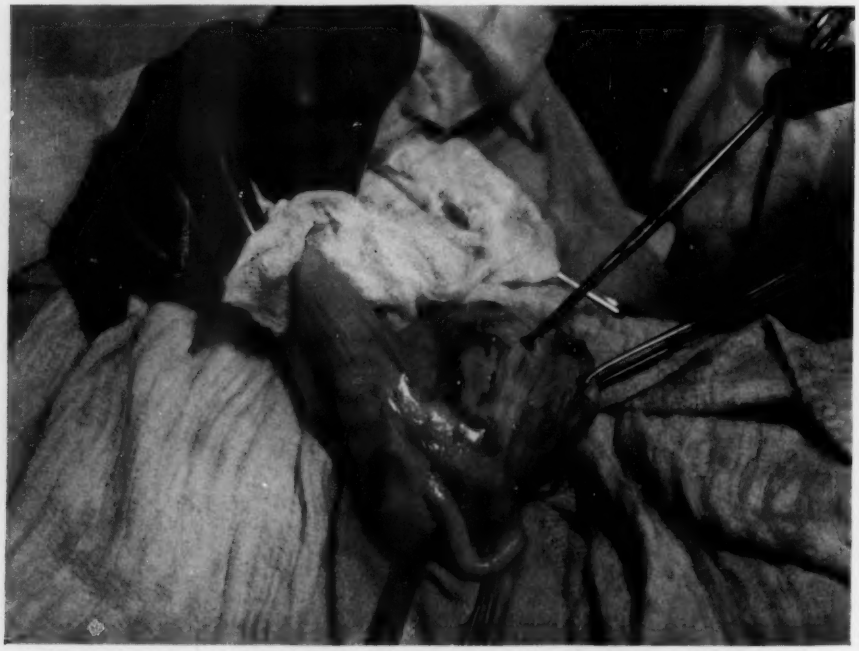


FIG. 3.—Enterogenous cyst at operation.

single layer of epithelium. In the deeper layer there were glandular structures lined by the same type of epithelium. There was fibrous and muscular tissue in the outer layers of the wall (Figs. 4 and 5). *Pathologic Diagnosis:* Enterogenous cyst arising from the terminal ileum.

The patient made an uneventful convalescence and was discharged, October 9, 1936. Two years later she was in excellent health.

Discussion.—It is not the purpose of this paper to discuss in detail the etiology, incidence, pathogenesis, *etc.*, of enterogenous cysts. Excellent reviews have been given by Evans,[3] Hughes-Jones,[1] and others. Suffice it to say that two theories have been advanced regarding the etiology of these cysts: (1) That they arise from diverticula of the intestine of the embryo; and (2) that the epithelium becomes detached from the embryonic intestine at a very early age and develops into a cyst. The cyst may occur anywhere along

the small or large bowel; however, of 55 cases collected by Hughes-Jones, 31 occurred in the region of the cecum and last four inches of the ileum.

With regard to the position of the cyst in relation to the wall of the intestine, it has been noted that the tumors in the jejunum and upper ileum are chiefly mesenteric in distribution, while in the ileocecal region, their incidence is greatest in the submucous and muscular layers. The tumors frequently show symptoms within the first years of life. They also occur more frequently in the female than in the male (3:2). The clinical manifestations of

FIG. 4.—Photomicrograph of section of the inner lining of the cyst. Note the epithelial lining and glandular structures in the deeper layer. (×65)

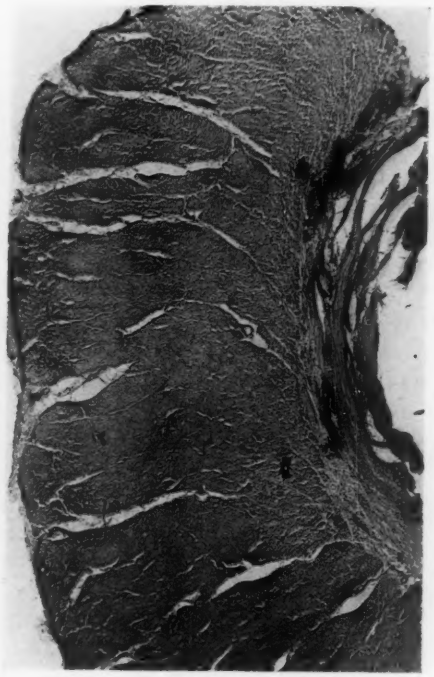


FIG. 5.—Photomicrograph of section of outer wall of the cyst, consisting of the muscular and fibrous tissue. (×200)

this condition are of special interest. According to the available literature, no case of enterogenous cyst has been diagnosed before operation. Most of these tumors give signs of intestinal obstruction. Of 34 cases collected from the literature by Hughes-Jones, the clinical picture of intestinal obstruction was present in 14, intussusception in six and volvulus in three. In some instances, the patient was thought to be suffering from appendicitis.

Our case is, apparently, the only one to have been reported in which contraction of the cyst was noted on physical examination. Millar and Robertson[4] describe a case of an enterocystoma, in which they believe the symptoms of vomiting and abdominal pain were due to temporary strong peristalsis of the patient's intestine which was shared by the cystoma. The fact that there may

be contraction and relaxation of the cyst, as observed in our case, lends credence to this view.

Treatment of this tumor consists in (a) enucleation; (b) excision of the bowel containing the cyst; (c) marsupialization; and (d) evacuation. Of these, enucleation is the procedure of choice. Hughes-Jones collected nine cases in which enucleation was attempted; five were successful and four were not. Miller[15] recorded ten instances of enucleation of cysts without a death, while he estimated the mortality from resection was 60 per cent. Marsupialization and evacuation of the cyst have been tried too few times to be evaluated, but theoretically these procedures would seem less desirable than removal of the tumor.

SUMMARY

A case of an enterogenous cyst arising from the terminal ileum in a female, age two, is reported. Contraction and relaxation of the cyst was noted on physical examination. Brief mention has been made of the etiology, incidence, clinical manifestations and treatment of this condition.

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CYST OF THE SEMILUNAR CARTILAGE*

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Although cysts of the external semilunar cartilages of the knee joint are no longer classed as rareties, very few of the mesial semilunar cartilage have been reported. A review of the more accessible literature revealed over 200 cases in all, reported prior to 1939. Among these, there are only 30 cases in which the lesion was in the internal cartilage.

There has been considerable controversy in the literature as to the etiology, physiology and pathology of these cysts. The etiology was accredited to trauma by a majority of the authors. Taylor[15] advanced some of the best evidence in favor of the traumatic theory as follows: There was a history of injury in 30 per cent of the cases. Seventy-two per cent of the cysts occurred in the middle third of the cartilage, which was relatively unprotected by the patellar ligament and the lateral ligament of the knee

A minority favored congenital or developmental origin. Ollerenshaw[12] particularly stressed the fact that although the internal cartilage was more frequently injured it was very infrequently involved by a cyst. He published a photograph of a cartilage removed from a female, age 11, in which the cyst was along the inner margin of the cartilage in the anterior third. He further cited instances of traumatic injuries with cartilage tears, in which a diagnosis of a cyst was made only upon removal of the cartilage. He reported several cases in which the cyst alone was excised; this recurred in every case.

In summing up the causes for cyst formation, Bennett and Shaw[1] found seven theories suggested by various authors: (1) Traumatic hemorrhage followed by mucoid degeneration of the hematoma. (2) Mucoid degeneration of the cartilage following trauma. (3) Injury to the blood or lymph channels producing a local change in the cell metabolism. (4) Obliteration of the paramenisceal arterioles causing degenerative changes in the cartilage. (5) Enlargement of certain cartilage cells with secretion of mucoid material into the connective tissue between them. (6) Trauma causing synovial implants in the cartilage. (7) Inclusion of synovia in the cartilage occurring during development.

Pathologically, the cysts were generally reported as multilocular, containing a gray to yellow gelatinous fluid. The stroma about the cysts was connective tissue. Most authors deny the presence of a lining to the cyst wall. Some recognize a flattened layer of connective tissue cells. A few (Ollerenshaw,[12] Kleinberg,[7] Zadek and Jaffe,[19] Satanowsky,[14] and Christmann[4]) reported an

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endothelial lining. Two authors (Venezian and Christmann[16]) described villus projections into the cyst cavity.

The case that we wish to present seems to fall into the developmental etiologic group.

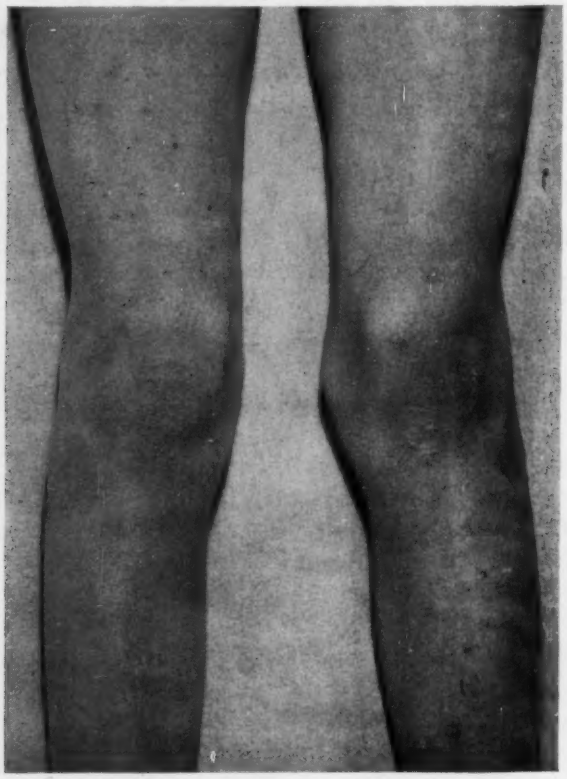

FIG. 1.—Objective appearance of a cyst of the left internal semilunar cartilage, in a female, age 8.

Case Report.—C. A., female, age 8, was examined December 2, 1938. A "lump" had been present on the inner side of the left knee for over a year. It had not noticeably increased in size. It gave no symptoms. There was no attributable cause. The medical history was irrelevant. On examination, a soft, fluctuant but firmly attached mass, approximately 0x1 cm., was palpable subcutaneously on the inner mesial side of the left knee (Fig. 1). Knee motion was full; there was no tenderness or swelling.

Operation.—January 12, 1939: A cystic mass was found, lying just anterior to the sartorius muscle and adjacent to the internal condyle of the femur. This was readily dissected free. As the joint space was approached, it was noticed that part of the internal lateral ligament was included in the wall of the cyst. With further dissection the joint space was opened and the cyst was found to be firmly attached to the internal cartilage. As dissection attempted to free the mass from the internal semilunar cartilage, a straw-colored, gelatinous, translucent fluid began to seep out. This indicated that the cartilage was involved. The tibial portion of the internal lateral ligament was found to include the distal portion of the cyst. This was dissected proximally to the joint cleft, and the cyst and internal semilunar cartilage were removed. The edges of the joint capsule were

plicated with silk sutures in an endeavor to substitute thickened capsule for the resected internal lateral ligament. The knee was immobilized with a plaster of paris bandage ap-

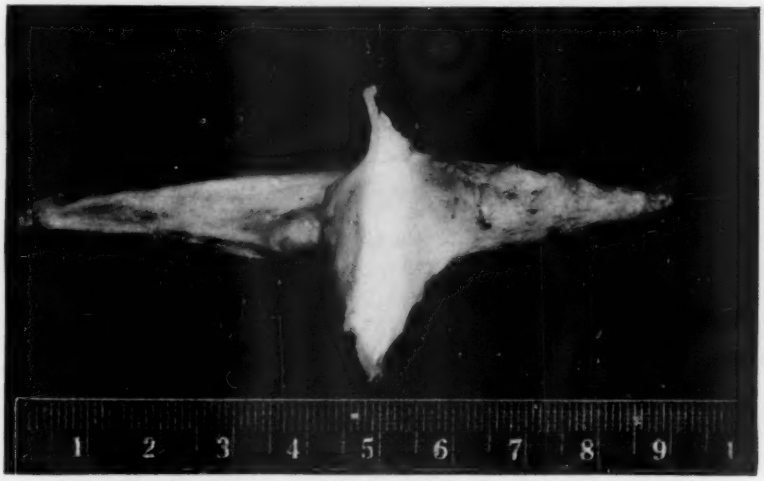

FIG. 2.—Photograph of the gross specimen (as viewed from the knee joint) showing the internal semilunar cartilage with the cystic expansion into the internal lateral ligament.

FIG. 3.—Photomicrograph showing a villus projection into the cyst cavity; an endothelial lining; the underlying connective tissue stroma; and the fibrocartilage of the meniscus.

plied next to the skin from ankle to groin with the joint at 180°, and in as much varus as possible.

Postoperative convalescence was uneventful. Muscle setting exercises for calf and

thigh groups were started the third day and weight-bearing the fifth. The plaster encasement was removed at the end of six weeks. There was no lateral mobility of the knee joint to indicate the loss of the internal lateral ligament. Active exercises against gravity were then instituted. In eight weeks there was full range of knee motion. Three months after operation the only difference in the two knees was the operative scar on the inner aspect of the joint and one-quarter of an inch atrophy of the thigh musculature on the left side.

Pathologic Examination.—Dr. Arthur Waltz, of the Children's Hospital, demonstrated that the cyst was multilocular (Fig. 2). It involved the periphery of the middle third of the internal semilunar cartilage and internal lateral ligament of the left knee joint. The loculations had extended parallel to the ligament fibers. Microscopically, the cyst cavity was lined with a layer of flattened endothelial cells practically identical with those lining the smaller blood vessels (Fig. 3). Beneath the endothelial cells was a connective tissue stroma. There were several villus projections from this stroma into the cyst cavity. These villi were covered with the same endothelial cells. Beneath the connective tissue stroma was found the fibrocartilage of the meniscus.

Discussion.—In the minds of the authors of this report, trauma does not account for the development of cysts of the semilunar cartilages. The age of this patient, age 8, and one reported by Colonna,[5] age 6, both without history of injury, would indicate a minimal influence from a traumatic cause. The typical multilocular character of the cysts reported would be against a traumatic dissolution of cartilage cells resulting in the formation of a cyst cavity. The absence of pigment precludes hemorrhage into cartilage resulting from an injury. The microscopic findings of villi and an endothelial lining would strongly indicate a developmental fault as the etiologic factor.

SUMMARY

Cysts of the internal semilunar cartilage are relatively infrequent. There is considerable diversity of opinion as to the etiology of cysts of the semilunar cartilages.

The case under consideration is that of a female, age 8, in which the cyst involved the internal lateral ligament as well as the fibrocartilage.

The microscopic examination revealed definite endothelial lining and villus projections within the cyst cavity.

The evidence in favor of trauma as the (sole) etiologic factor is wanting.

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LOCKING ATTACHMENT FOR THE BALFOUR RETRACTOR

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MOST SURGEONS using a Balfour retractor, particularly if the instrument has been in use for some time, have experienced the inconvenience of having the movable blade continually slip and relax the tension on the sides of the wound. A common practice is to tie a piece of gauze over the end of the instrument and around the movable blade to hold it in position.

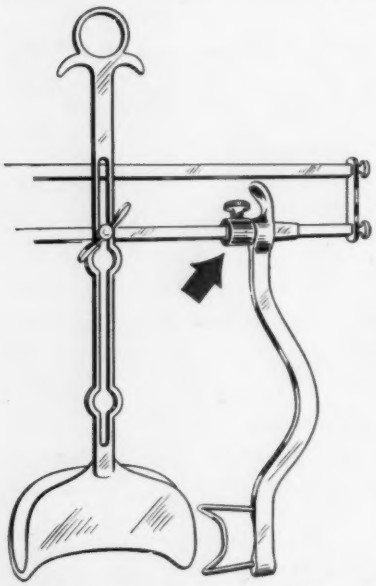

FIG. 1.—Attachment on retractor indicated by arrow.

This difficulty has been overcome by employing a simple device: The apparatus consists of a chrome-plated brass collar and set screw. The collar is approximately three-fourths of an inch in diameter and one-half inch long, with a square hole large enough to be a free fit on the sleeve (Fig. 1). The set screw with knurled or wing-head is so designed that it will not back out and get free from the collar. This screw also locks the collar on the sleeve. A small hole the size of the screw should be drilled through the sleeve so the screw comes in contact with the bar. Since the movable blade of the retractor was designed to hold by friction, only a gentle pressure of the set screw is necessary to maintain the blade in position.

We have used this device repeatedly and have found it very satisfactory.

Submitted for publication August 18, 1939.

BOOK REVIEWS

THE TREATMENT OF WAR WOUNDS AND FRACTURES. By J. TRUETA, M.D. New York: Paul B. Hoeber, Inc., 1940.

THIS AMPLIFICATION of a small manual, which was published during the war in Spain, first in Catalonian, and later in Spanish, the author says, is the result of a demand not only from surgeons, but also the general practitioners who have been called upon during the military emergency to face the necessity of acquiring knowledge which they formerly had been content to regard as belonging to the surgeon. Though this expanded version is published after the close of the Spanish War, and "at a time when the world is at peace" (???), he is convinced that open fractures of civil life, road accidents, and those of industry do not differ essentially from those produced by aerial bombs, falling masonry, *etc.*, and that the fundamental treatments ar essentially the same, whatever may be the cause. He reveals in this book the necessity for keeping the word "war" in the title, for the subjects dealt with include the collection, transport, and evacuation of casualties, together with the treatment of neglected cases. Particular attention is given in this volume to a new problem of the present type of warfare, namely, the mass attacks directed against densely populated cities.

A report based upon his personal experience with a total of 1,073 cases of open fractures of the limbs, with but six deaths, demands that surgeons "stop, look and listen" at this time of impending world war. The almost uniform and simple methods of treatment of compound fractures, consisting of immediate débridement after reduction of the fracture, and immobilization in a plaster encasement, have certainly proven, in his experience, of special value in war-time.

The war in Spain provided the opportunity for a successful, large-scale study of the method, but the results of the study are certainly available for the benefit of victims of transport and industrial accidents in time of peace. Some 20,000 cases were treated by the same method, but detailed statistics of the results are not available at the present time. Trueta believes that the experiment was on a sufficiently large scale to justify the belief that the methods of treatment employed were responsible for his unbelievably low mortality. To add to this, among the bad results obtained, some 91, only four required amputation. To those who were engaged with the surgical care of the injured in the first World War these figures seem almost impossible.

The experience reported covers over 30 months of continual treatment of war casualties, including the immediate surgical treatment of casualties in 300 air raids. By rapid, properly planned, and boldly executed surgery, first advocated by Winnett Orr, followed by closed plaster of paris encase-

ment, the casualties can be spared the torment of having to spend the rest of their days crippled and mutilated.

Trueta feels that, in his experience, all the failures of the closed method of treatment of wounds are due to a failure to appreciate the general principles. Closed treatment should be employed only by those qualified by training to plan and undertake the first stages of the technic of débridement—which are purely surgical. It is completely falacious, he warns, to believe that it suffices to close a wounded limb in a plaster of paris encasement to achieve the benefits of the closed treatment.

The book, which is pocket size, promises to become a testament not only to those who may in the future be called upon for duty in the medical corps of the armies, but also for those who may be engaged in traumatic surgery in civil practice.

It contains chapters on the historic survey of the development of military surgery, starting with Ambroïse Paré and including the war of 1914–1918. It pays due credit to Orr, who, as a result of his experience in the World War, evolved the principles of treatment, which consist in: (1) The importance of rest for the healing of wounds of soft tissues and bones; (2) the prevention of access of infected organisms to the tissues; and (3) immobilization, so that pain is reduced to a minimum and healing is allowed to proceed. No one at the present time can take issue with his first principle of débridement, nor with the second one of the removal of dead and infected tissue, and the prevention of the introduction of further infection. However, the use of the plaster encasement for immobilization has not been generally accepted, and he offers a summary of his reasons for believing that this is an essential factor in the Orr treatment:

(1) Rest allows local venous and capillary thrombi to form. These prevent and delay the spread of infection and are not broken down by repeated handling.

(2) Rest allows new capillaries to form which are not torn by repeated dressings of the wound.

(3) The plaster maintains a constant beneficial pressure on the wound; the calcium in it may be of local value.

(4) The mixture of organisms on the wound may by their mutual antagonism prevent the victory of any one group.

(5) To leave the wound uncovered, as advocated by Schede and Bohler, is good treatment for superficial wounds; but in the deep wounds produced by shells and aerial bombs, the dehydration and loss of heat which results from this treatment induces a condition of shock inimical to the general well-being of the patient and to the healing of his wounds.

This is truly a remarkable contribution, not only to military surgery, but to traumatic surgery. When the authenticity of this report is vouched for by such men as Matas and Eloesser it can be accepted at par value.

WALTER ESTELL LEE.

"HARVEY CUSHING'S SEVENTIETH BIRTHDAY PARTY." Published for the Harvey Cushing Society by Charles C. Thomas, Springfield, Illinois, 1940.

THE PRESENTATION in book form of the occasion of "Cushing's Birthday Party" has been made possible by the combined efforts of the Harvey Cushing Society and Charles C. Thomas, Publishers, and provides an opportunity for his innumerable friends, students and admirers, outside the circle of the Cushing Society, to share the many tributes offered to this outstanding figure of American Surgery during the twentieth century.

As stated in the preface, it is "Hail and Farewell," for while this tribute was in press Doctor Cushing died.

> "All things we ordain festival
> Turn from their office to black funeral."

Truly the present and future generations should feel indebted to the Cushing Society for preserving the warmth, gayety and intimacy of that occasion, for it was a remarkable event.

The quotation from a letter received from the President of the United States is typical of this intimate friendship that was the spirit of the party:

"The spirit of eternal youth is his. It is not only his good fortune but the good fortune of all those who are privileged to call him a friend. I think, too, it accounts for the fact that there has been no slowing down in his zest for life and for his work—a work which makes the human race his debtor and which has won him the plaudits of the great and the eternal gratitude of all sorts and conditions of men."

The volume includes not only the speeches given at the dinner, April 8, 1939, but also selections from letters and telegrams received by Doctor Cushing, together with a number of appreciations from the lay and medical press. Further, there is an account by Dr. Henry Viets of Doctor Cushing's case records written while he was an intern at the Massachusetts General Hospital, which deserves more than passing mention, for in these case histories there is definite evidence, at the beginning of his career, of the characteristics of a great man and a genius.

To the six independent publications which have been previously issued in connection with "Cushing's Birthday," and as a supplement to his bibliography, this volume is a worthy companion, and should be in the library of every American physician and surgeon. The intimacy of the tributes paid by his students and associates should and will serve as an inspiration to future generations, and no doubt will provide the nucleus for some Boswell to write a "Life of Harvey Cushing" comparable to the one which he wrote of Sir William Osler.

WALTER ESTELL LEE.

SHOCK: BLOOD STUDIES AS A GUIDE TO THERAPY. By John Scudder, M.D. Philadelphia, J. B. Lippincott Co. 1940.

THE AUTHOR'S premise for the subtitle, "Blood Studies as a Guide to Therapy," may be stated very briefly. Two events, occurring separately or together, explain the circulatory failure in shock; loss of blood *in toto*, and the large obstacle to blood flow caused by a loss of blood plasma. Blood may be lost by hemorrhage or, according to accredited theory, by being trapped in its capillary bed by vasoconstriction. Loss of blood plasma may be caused by processes of dehydration, or by vasoconstriction, or, in the case of burns, by loss of proteins from the vascular compartment. A correct choice of reparative measures obviously requires appraisement of these various components of circulatory collapse. To this end, examination of the peripheral blood is clearly indicated. The author quite convincingly demonstrates the serviceableness of specific gravity measurements by the simple and rapid falling-drop method of Barbour and Hamilton. A measurement of whole blood specific gravity is often adequately informative. A more dependable definition of the underlying circumstances is, however, obtained by an hematocrit measurement using heparinized blood, and then determining the specific gravity of the plasma from the sample. Except as modified by hemorrhage, these measurements usually demonstrate hemoconcentration, or, in words more significant as regards circulatory failure, reduction of blood plasma volume. The utility of these simple measurements as a means of indicating therapeutic agents and observing their effectiveness is thoroughly illustrated by a large series of case records. Although their helpfulness is clearly demonstrated, the reader will not be surprised to find that the analysis and treatment of shock is not yet a rule of thumb procedure and for this reason remains an entertaining problem, for the contemplation of which these detailed records supply an excellent framework and the incentive of appraisement of the author's use of the evidence. The reader will profit greatly by studying them carefully. Here, in addition to replacement therapy, he will find applied the newest agent of plasma volume control; extract of the cortex of the adrenal gland; a probably reasonable experiment in therapy even though direct evidence of failure of function of the adrenal cortex in shock is lacking. The author, being aware that examination of the peripheral blood will not define the *extent* of blood and extracellular fluid losses, has emphasized the well established requirement for estimation of the position of body fluid balance in situations which have produced shock.

The book is much more extensively informative than the subtitle suggests. It is also an excellent "guide" to the historic and experimental development of current conceptions of shock, with a proper emphasis on the relationship of body fluid disturbances to circulatory failure. In this direction a résumé of the functions of the adrenal cortex is included.

A large item in the book is the author's advocacy of plasma potassium increase for a prominent position in the pathogenesis of shock. The premise

used is a vasoconstrictive action of potassium and a deleterious effect on the heart. The author presents a large amount of evidence in support of his accusation of potassium. All of it is, however, entirely circumstantial. Direct proof that the levels of plasma potassium found in patients in shock cause either vasoconstriction or cardiac embarrassment is not provided. Study of the data presented does not at all convincingly describe a relationship of potassium concentration to degree of shock. Increase in plasma potassium is easily understandable as a result of disturbance of extra- and intracellular fluid adjustments. That it has an especial significance among many concurrent distortions of the plasma structure and changes in the physical properties of the blood is obviously difficult of proof. By the same token, the author's indictment of potassium cannot be dogmatically denied. At any rate since, as the author admits, vasoconstriction as evidenced by hemoconcentration precedes the accumulation of potassium in the plasma, potassium is clearly not the long sought agent of that basal happening. But denying potassium a primary rôle does not remove the important question which the author has raised of its position among the many circumstances which determine the eventual outcome in shock. The above comments are intended only to indicate the intricacies of this problem and the unwillingness of this reviewer to be convinced by the evidence at hand.

JAMES L. GAMBLE.

DIVERTICULA AND DIVERTICULITIS OF THE INTESTINE. Their Pathology, Diagnosis and Treatment. By HAROLD C. EDWARDS, M.S. (Lond.), F.R.C.S. (Eng.). Surgeon and Lecturer in Surgery to King's College Hospital, London. With Foreword by Gordon Gordon-Taylor, O.B.E., M.S., F.R.C.S. With 223 illustrations, many in color. William Wood Medical Books, Baltimore, 1939.

This work is in substance the Jacksonian Prize Essay of the Royal College of Surgeons for the year 1932, revised and brought up to date. It represents the result of a personal investigation of clinical cases, the data of which were obtained from the case histories of patients suffering from symptoms due to the presence of diverticula, or in whom diverticula were found at operation, postmortem, or revealed during a roentgenologic examination. The majority of these cases were examined personally. In addition, a questionnaire was circulated to all patients in whom diverticula were found roentgenologically.

The pathologic specimens are from various sources. Some are recent operative specimens from the author's own cases or those of colleagues. For most of the cases in the unusually rich series of colovesical fistulae, the author is greatly indebted to the late Sir John Thomson-Walker, who furnished him with the notes of many of his private cases. Others have been obtained at postmortem examinations performed during the past 16 years. A number are from museum shelves. All these have been taken out of their bottles for re-

investigation. The author is indebted to the curators of museums other than that of his own school for the loan of some of the specimens examined and described in the text.

The roentgenographic material is derived chiefly from King's College Hospital during the period 1925–1937, inclusive. A few only of the prints were obtained from colleagues and other sources.

There are numerous excellent articles available in the American surgical literature dealing with the frequency of diverticula, their probable etiology and their treatment. A student, however, has some difficulty finding a monograph dealing with the subject in a comprehensive manner. Doctor Edwards' book is, therefore, timely, but would have been of still greater value if it had included diverticula of the entire alimentary canal.

In the introduction the author deals with the classification of diverticula. He divides them into congenital and acquired. The first group is composed almost exclusively of Meckel's diverticula to which he adds a few other rare congenital diverticula not of Meckelian origin. The second, or acquired, group is subdivided into those arising from the duodenum, jejunum and ileum, colon and vermiform appendix.

Section I deals with the congenital types. The subject is well presented especially in regard to the clinical significance of pathologic conditions which may affect Meckel's diverticulum.

Section II is devoted to diverticula of the duodenum. It calls attention to the increased frequency with which this condition is being reported, apparently due to improved radiologic technic and interest in the subject. The radiologic appearance of these lesions is well illustrated. One slide shows a microscopic section indicating the protrusion of the diverticulum between muscle fibers, and thereby presents evidence of being acquired rather than congenital in nature. This point is further emphasized in special chapters on morbid anatomy and pathogenesis, which present a critical discussion which is recommended to those interested in the subject. The author further calls attention to the frequent association of duodenal diverticula and diverticulosis of the colon, and believes that, because the morphology and age incidence are identical, the same factors are responsible for their development. A special chapter devoted to ulcer-diverticula of the duodenum is very interesting and well illustrated. In the chapter on operative technic, he justly calls attention to the dangers involved, and describes the technic advocated in diverticula affecting the different portions of the duodenum. The value of this chapter to the reader would have been increased by a discussion of indications for operation. This phase is but slightly touched upon in Chapter X under the heading "The Clinical Aspect."

Section III is well illustrated with a wealth of clinical and postmortem material pertaining to diverticula of the jejunum. The chapter on pathogenesis is excellent. Although the condition is held to be relatively uncommon and of little clinical importance, complications of perforation, acute diverticulitis,

acute obstruction and volvulus are described. Medical and surgical treatment is discussed.

Section IV deals with diverticula of the large intestine, including the appendix. It comprises about half the book—which is in accordance with the clinical importance of these lesions. The author presents interesting statistics on incidence which, in general, correspond to those observed in this country. He shows, on the basis of anatomic and microscopic material, that these diverticula emerge at the points of entry of blood vessels. There are beautifully colored illustrations showing the early stage of development. Considerable attention is paid in Chapter XXII to the radiologic aspect, and it is richly illustrated. Treatment of diverticulosis and uncomplicated diverticulitis is medical, which consists of the prevention of stasis in the diverticula. The methods employed are avoidance of constipation, reducing the bulk of undigested and indigestible food and colon lavage. Indications for operation are discussed in those uncomplicated cases with persistent symptoms, recurrent exacerbations, and persistence of bladder symptoms. The various operative procedures which may be utilized are presented.

Diverticulitis with complications is discussed in detail, together with the different operations which may be employed during the acute stage of perforation or for one of the later sequelae.

Among 162 cases of diverticula of the colon, nine were associated with a new growth (5.6 per cent).

The final chapter is devoted to diverticula of the vermiform appendix, and is followed by a very complete bibliography.

The review of this excellent book has been instructive and profitable and it is unhesitatingly recommended to physicians as well as surgeons.

CARL EGGERS.

MEMOIR

GEORGE W. W. BREWSTER

1866–1939

GEORGE W. W. BREWSTER died suddenly at his home in Boston, September 26, 1939, in his seventy-fourth year. He was born in Roxbury, Massachusetts, March 26, 1866, and prepared for college at the Roxbury Latin School. He was graduated from Harvard College in the class of 1889, and received his M.D. degree from the Harvard Medical School in 1893. He served as surgical intern at the Massachusetts General Hospital following his graduation, and soon afterwards became private assistant to Dr. Maurice H. Richardson. He was one of the first of the group of distinguished assistants of a distinguished master, and ever after gratefully acknowledged his indebtedness to that great teacher of sound surgical principles.

In 1900, he was appointed Surgeon to Out-Patients at the Massachusetts General Hospital, becoming Assistant Surgeon in 1906, and Visiting Surgeon in 1914. In 1927, at the completion of 27 years of active surgical service, he reached the retiring age at that hospital and was appointed to the Board of Consultation. He was also surgical consultant to the Chelsea Memorial Hospital, Chelsea, Mass., Leonard Morse Hospital, Natick, Mass., Milford Hospital, Milford, Mass., and Beth Israel Hospital, Boston, Mass.

He carried on an active surgical practice until within the last few years when increasing ill health incapacitated him for such taxing work. He bore the heavy burden of a distressing chronic ailment with great fortitude and cheerfulness.

He is survived by his widow, Ellen Hodge Brewster, and three sons: William L., George W. W., Jr., and Henry H., M.D.

George Brewster was a lineal descendant of Elder William Brewster who came over in the Mayflower and landed on the Rock at Plymouth. The mellowing influences of time, space, and freedom in the New World have happily softened, in their prolific progeny, some of the granitic qualities of the early Puritans, notably their austerity and intolerance, but the sterling underlying qualities of character and purpose of the Fathers are clearly discernible in the salient traits of this son of that hardy stock.

George Brewster loved with the utmost loyalty his family, his profession, and his friends—all that made his life.

He was a clinical surgeon of great ability and skill. His diagnostic acumen acquired before the days of roentgenology and elaborate laboratory tests seemed intuitive and almost uncanny. His judgment was sound, and he knew both how and when to operate and when to withhold his hand. In acute abdominal emergencies he was perhaps at his best. Quick, deft, and unhesitating,

he went direct to the lesion with the least possible damage to surrounding tissues. He excelled also in the delicate surgery of the neck and thyroid gland. His interest in the patient did not cease with the operation—he took infinite pains with the after-care, and knew how to make a sick man comfortable and happy. The most forlorn ward patient would smile at his approach.

GEORGE W. W. BREWSTER, M.D.

He was free from every affectation except one harmless one; he delighted in pretending to be completely at a loss as to how to proceed in the midst of an operation in order to draw out some ingenuous advice from an unwary assistant. He hated sham and pomposity and was an adept at exposing the one, and deflating the other, with outspoken candor. His frankness at times was

almost appalling but no one could take legitimate offense when the intent was always kindly.

He was immensely popular with his fellow-man, and belonged to many professional societies and social clubs: He was elected to the American Surgical Association in 1917. There never was a more loyal member, or one who enjoyed the meetings more than he, and none received a warmer welcome from their many friends than Dr. and Mrs. George Brewster. He was not a frequent contributor of papers but he followed the presentations of others with keen interest and extraordinary patience, his comments, not from the platform, but in a low tone to his intimates on the seats, were succinct, to the point, and usually appreciative.

He never occupied a professorial chair, but as an unacademic teacher of good, sound surgery he deeply influenced a very considerable group of students, interns, assistants and consultants who cherish the memory of his dynamic sayings and brilliant demonstrations. Brought up as he was in the older school of what is now regarded as rough and ready surgery, he always kept an open mind, and was keenly interested in, and receptive to, the newer advances.

He liked young men and followed their careers with genuine interest. He loved the old M.G.H.; and up to the very end, was almost a daily visitor at clinics and staff conferences, where his genial presence and sound criticism and advice were always welcome. He was greatly beloved by young and old, he never grew old himself, he was unique, he did great good in the world, and is sorely missed by a host of friends. May his genes endure.

LINCOLN DAVIS.

EDITORIAL ADDRESS

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